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DRUG ERUPTIONS

I. FIXED PHENOLPHTHALEIN ERUPTIONS

FRED WISE, M.D.

AND

MARION B. SULZBERGER, M.D.

NEW YORK

In employing the term "drug eruptions" in this paper, we intend to use the expression in a purely etiologic sense; that is, we include all cutaneous manifestations due to substances used as medicaments regardless of whether they are synthetic or derived from nature, or whether they are pure chemicals or mixtures. For the purposes of our presentation we further disregard the manner of contact with the drug, whether it has been used internally or externally. We also embrace within our definition all the various clinical types, including eczematous eruptions (as from quinine or butesin picrate), fixed eruptions (as from phenolphthalein, antipyrine or arsphenamine) and acneform eruptions (as from iodine or bromine).

While we realize that such a classification is arbitrary, we believe it logical, perhaps just as logical as the designation of syphilis for the variegated manifestations of syphilitic infection, or of tuberculosis for the polymorphous pictures caused by Koch's bacillus.

There are some points, however, at which the division that we make is forced. For instance, quinine dermatitis is here included, whereas primrose dermatitis, rhus dermatitis or cocabola dermatitis, if caused by chance contact, although essentially identical processes and also due to plant derivatives, do not come within the definition. However, such more or less unnatural cleavages are necessary for the sake of clarity.

It will be seen that our definition does not exactly correspond to dermatitis venenata or to dermatitis medicamentosa, as both of these terms connote the manner of contact, the former implying external application and the latter internal administration. We repeat that we are merely defining "drug eruption" as we shall use it in this study; we are not attempting a new classification.

From the Department of Dermatology and Syphilis, New York Post Graduate Medical School of Columbia University.

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It is, of course, impossible for us to give a complete survey of, or an exhaustive bibliography on, the entire subject. This seems unnecessary, as there is a chapter dealing with drug eruptions in Jadassohn's "Handbuch der Haut- und Geschlechtskrankheiten." [1] In this communication, therefore, we shall touch on previous work only when it is necessary for the understanding of our clinical observations and experiments or their theoretical discussion.

Nearly all drug eruptions are idiosyncrasies, reactions of sensitization, generally not to be identified with and entirely different from the pharmacologic effects of the causative drug or the results of poisoning from overdosage. They may be of many different types, and in some persons two or more types may be combined. As some of the cardinal forms, and the drugs most commonly causing them, we wish to enumerate only the following:

1. Truly eczematous eruptions with erythema, vesiculation, weeping and scaling (quinine, procaine hydrochloride, ephedrine, mercurials, sometimes arsphenamines, etc.).

2. Urticarial eruptions (belladonna, atropine, the morphine group, phenolphthalein).

3. Scaly erythematous eruptions, purely erythematous or scarlatiniform, and morbilliform and dermatitis exfoliativa-like conditions (arsenic, arsphenamine, belladonna, balsams, the heavy metals).

4. Erythema multiforme-like eruptions (phenolphthalein, antipyrine, salicylates).

5. Erythema nodosum-like eruptions (iodides, bromides).

6. Acneform, furunculoid and erysipelas-like eruptions (bromides, iodides, chlorine, oils and tars, etc.).

7. Ulcerating and vegetating eruptions (bromides, iodides).

8. Purpuric eruptions (iodides, arsphenamines, particularly sulpharsphenamine, balsams).

9. Fixed and circumscribed, erythematous or bullous and polychromatic pigmented eruptions (phenolphthalein, antipyrine and sometimes the arsphenamines).

In the two first categories, eczemas and urticarias, the mechanism of sensitization and the site of sensitivity have been extensively studied, and knowledge has been enriched in recent years. They are essentially eczematous and urticarial reactions, of the same nature and type as those due to other causes. The route both of sensitization and of elicitation of reaction has been well described for the eczematous form by Jadassohn.[2] Sensitization may take place from within or from with-

1. Mayer and Kleeberg, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, to be published.

2. Jadassohn, J.: Bemerkungen zur Sensibilisierung und Desensibilisierung bei den Ekzemen, Klin. Wchnschr. **21**:1680, 1923.

out;[3] contact with the substances causing the eruption may likewise be of external or of internal origin. There are thus the following possibilities:

Sensitization Brought About	Reaction Caused
1. From within	From within
2. From within	From without
3. From without	From within
4. From without	From without

We shall cite examples of these different methods from actual cases.

M. C. was given large doses of methenamine for cystitis; toward the end of this treatment an eczematous dermatitis developed which healed after discontinuance of the drug. We saw the patient some time after this, when we were consulted on account of a dermatophytosis of the groin (perhaps due to previous sensitization to formaldehyde and ensuing polyvalence, embracing fungous products [?]). We made routine patch tests, among them one with a dilute solution of formaldehyde (5 per cent). This was strongly positive. (The patient was an elderly woman; had she been a laboratory worker and come in contact with formaldehyde, it is probable that she would have had dermatitis venenata from this substance.) This is a case belonging to group 2 (sensitization from within, to contact from without) and also to group 1, as the previous dermatitis recurred on repeated internal administration of methenamine (which, as is well known, splits in an acid medium, forming formaldehyde).

An example of the opposite sequence is given in the following case, in which the sensitization took place from without and a later reaction was elicited from within (group 3).

A year prior to this report a woman, aged 22 (E. L.), an employee of a hairdressing establishment, presented herself at the Post-Graduate Skin Clinic because of an eczematous, weeping dermatitis of the scalp, face, eyelids, neck, hands and arms. She had employed a "dandruff cure" for several weeks previous to the outbreak. On investigation it was proved that the preparation contained quinine, and a patch test with it and with a 1 per cent solution of quinine hydrochloride were both strongly positive. The patient was warned against contact with lotions and other articles containing quinine. She remained free from eruption for one year. On April 6, 1932, she again appeared at the clinic. She had an eczematous eruption which covered her skin from head to foot. This had appeared within three hours after ingestion of a "bromoquinine laxative" tablet. The generalized eruption healed, but the sites which had been affected by the previous eruption due to external application healed much more slowly than the other areas, and isolated eczematous patches on the hands, arms, forearms, scalp, face and neck were present many weeks after the remaining skin had completely healed. A patch test with quinine was again strongly positive, while other substances, including bromides, caused no reaction (case reported in detail by Bloch[4]).

3. This remark also applies to desensitization.

4. Bloch, B.: The Rôle of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:175 (Feb.) 1929.

There are many examples of other modes of sensitization and causation. Dermatitis following the application of ointments, lotions and similar preparations is most frequently an instance of group 4, and the eruptions following the ingestion of phenolphthalein and of other drugs are usually examples of group 1.

Some arsphenamine eruptions are probably examples of group 3 (sensitization through inadvertent paravenous injection and deposit in the cutaneous tissues; see Klauder,[5] Frei and Mayer,[6] Sulzberger,[7] Schoch [8]).

Before leaving this aspect of the question, we should like to call attention to an eventuality of importance in practical work, namely, that all of such sensitization may become polyvalent (Bloch [9]). In this way a sensitization from within or without may cause a patient to react to other drugs or substances, whether of internal or of external origin. In this way, for instance, tinea infections, which often cause eczematous sensitization to fungous products, may also cause sensitizations to drugs or other substances in two ways: first, through the polyvalent broadening of the sensitivity to include drugs in addition to trichophytin, and, second, through the injury to the skin caused by the tinea process which permits the penetration and intimate contact of applied medicaments and other substances. Such breaches of continuity of the epidermal covering and damage to the skin favor sensitization. We shall present additional evidence of this in a group of cases of butesin picrate dermatitis reported in the second paper of this series.[9a]

Just as the mechanisms of sensitization have been assiduously studied in eczematous eruptions, the questions of the site of sensitiveness and the localization and the type of the shock tissue have been thoroughly examined. We refer to the work of J. Jadassohn, Bloch, W. Jadassohn [10]

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5. Klauder, J. V.: Hypersensitiveness to Local Contact with the Arsphenamins Producing Chronic Eczematoid Dermatitis and Asthmatic Symptoms, Arch. Dermat. & Syph. **5**:486 (April) 1922.

6. Frei, W., and Mayer, R. L.: Versuch einer chemischen Analyse der Hautueberempfindlichkeit nach Salvarsandermatitiden, Arch. f. Dermat. u. Syph. **153**:606, 1927.

7. Sulzberger, Marion B.: Hypersensitiveness to Arsphenamins in Guinea-Pigs: I. Experiments in Prevention and in Desensitization, Arch. Dermat. & Syph. **20**:669 (Nov.) 1929; Arsphenamine Hypersensitiveness in Guinea-Pigs: II. Experiments Demonstrating the Rôle of the Skin Both as Originator and as Site of the Hypersensitiveness, ibid. **22**:839 (Nov.) 1930.

8. Schoch, A. G.: Arsphenamine Sensitization Tests, Am. J. Syph. **14**:75, 1930.

9. Bloch, B.: Pathogenese des Ekzems, Arch. f. Dermat. u. Syph **145**:34, 1924.

9a. Sulzberger, Marion B., and Wise, Fred: Drug Eruptions: II. Certain Further Observations, Dermatitis Eczematosa, to be published.

10. Jadassohn, W.: Die Immunbiologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 353.

and others for a more detailed discussion of this phase of the subject. Suffice it to state that it is now the consensus that the epidermis (and perhaps the topmost vascular layers of the cutis) are the site of the first reaction. The epidermis itself is sensitized and either is the first tissue to react or reacts very early in the process.

Less is known concerning the manner of sensitization in the second group of drug eruptions, namely, those of urticarial type. It is probable that what we have said concerning the eczematous eruptions applies also to the urticarial group, with the exception that in most cases it seems necessary for the epidermis to have a break in continuity in order that an urticarial reaction be produced by a substance applied to the skin from without. (Patch tests do not usually cause urticarial reactions even in subjects with a very strong urticarial type of hypersensitiveness. On the other hand, in such patients a superficial scratch before the application of the substance suffices to elicit the wheal and flare response.)[10]

The opinions concerning the intervention of demonstrable antibodies in urticarial drug eruptions are not in agreement. Much more work is necessary before definite conclusions concerning this can be reached. Neither cutaneous tests nor passive transference experiments have proved as successful in the urticarial drug eruptions as they have in asthma, hay fever or neurodermatitis disseminatus. Frequently the nature of the causative drug prevents successful or exact investigation in this direction. The drugs causing urticaria are often either almost insoluble in water (phenolphthalein) or the primary causes of urticarial reaction which, when applied in the proper manner even to normal, nonhypersensitive areas of skin, elicit an urticarial response (atropine, morphine).

There is much more definite knowledge available concerning the seat of the urticarial reaction which is today generally conceded to be the capillary and precapillary blood vessels of the uppermost cutis (for detailed discussion of this subject see Lewis[11] and W. Jadassohn[10]).

In many of the other forms of drug eruptions that we have listed, knowledge on the points discussed is exceedingly limited. This is particularly true in group 9, comprising the fixed circumscribed eruptions, a comparatively rare type. The drugs which most often cause this type of eruption are phenolphthalein and antipyrine, the former much more frequently than the latter. On account of the widespread use of phenolphthalein in America and its relatively infrequent use in Europe, American dermatologists are placed in a favorable position for the discovery of new facts concerning this type of hypersensitiveness. Each case of this type which is available for study should be utilized,

11. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw and Sons, Ltd., 1927.

and we urge that dermatologists in a position to do so make thorough histologic and histochemical examinations of the tissues in these cases, including dioxyphenylalanine reactions, nerve stains and impregnations. References to histologic observations are very sparse in the literature, and to our knowledge no special investigative technics have been employed. As there is naturally a limit to the number of biopsies and experiments that can be performed in each case, we were not able to study this aspect of the problem.

FIXED PHENOLPHTHALEIN ERUPTIONS [11a]

The first question which we attempted to approach was that of the demonstration of the site of sensitivity in the fixed phenolphthalein eruptions, and for this purpose we carried out the following experiments on the three patients available. All of these clinically presented typical examples of the fixed, circumscribed phenolphthalein eruption, proved to be due to this drug both by the history of the dermatosis following ingestion of phenolphthalein and by the experimental reproduction of the eruption by means of administration of the drug by mouth.

EXPERIMENT 1.—The following solutions were prepared:

(*a*) A 2 per cent solution of white phenolphthalein in 70 per cent alcohol.

(*b*) A 2 per cent solution of yellow phenolphthalein in 70 per cent alcohol.

(*c*) A freshly prepared mixture of one part of solution (*a*) and two parts of physiologic solution of sodium chloride.

(*d*) A freshly prepared mixture of one part of solution (*b*) and two parts of physiologic solution of sodium chloride.

Patch tests with solutions (*a*) and (*b*) were negative in all three cases, both on normal and on previously affected areas of skin. Intradermal tests with injections of 0.1 cc. each of solutions (*c*) and (*d*), both in the previously affected areas and in normal skin, caused slightly infiltrated and reddened papules varying in size from that of a lentil to that of a small pea to appear within from twenty-four to forty-eight hours after injection. The reaction in the previously affected areas was no greater than in the normal skin.

Patch tests performed in the same manner on eight controls (adults suffering from other diseases of the skin) were negative, except in T. H., a woman, aged 23, who was being treated for an eczematous eruption of the hands (dermatophytid?). In this patient there was a definite eczematous reaction at the site of the test, with erythema, scaling and infiltration which were stronger at the site of injection of solution (*b*). At this site there was also some vesiculation.[12]

11a. For descriptions of clinical varieties see Wise, Fred, and Abramowitz, E. W.: Phenolphthalein Eruptions, Arch. Dermat. & Syph. **5**:297 (March) 1922.

12. We are at a loss for a definite explanation or interpretation of this reaction. We believe, however, that we may conclude from this that phenolphthalein eruptions of eczematous character must be considered as possibly resulting from the ingestion of phenolphthalein, as the reaction proved that this form of hypersensitiveness to the drug exists. What was apparently such a case with positive patch tests was recently reported by Bernstein (Bernstein, F.: Ueberempfindlichkeit gegen Phenolphthalein, Dermat. Ztschr. **62**:366 [Dec.] 1931).

Intradermal injections of solutions (*c*) and (*d*) in five control subjects caused either small, scarcely visible papules which appeared within from twenty-four to forty-eight hours after injection or no reactions. These papules seemed smaller than those in patients who had been given phenolphthalein, but we should not like to draw far-reaching conclusions from this apparent difference. The number of cases observed is too small, and the reactions were not all viewed side by side at the same time, nor were accurate measurements possible.

No immediate wheal reactions could be elicited with solutions (*c*) and (*d*), either in patients who had been given phenolphthalein or in controls.

Conclusions.—The existence of eczematous hypersensitiveness could be demonstrated neither in normal nor in previously affected skin in three cases of fixed phenolphthalein eruptions. No urticarial hypersensitiveness could be shown in these cases, and no late papular type of hypersensitiveness could be proved to exist. These results speak against the epidermis or the superficial layers of the cutis as being the seat of this form of hypersensitiveness. Intradermal tests must be continued in a larger series of patients and at varying intervals.

EXPERIMENT 2.—A. L., aged 46, presented himself at the Post-Graduate Skin Clinic on January 28, 1932. He gave a history of having taken tablets containing phenolphthalein and of recurrent cutaneous eruptions during five or six years. General examination gave negative results. This otherwise robust, healthy man presented the following lesions: a typical eruption of round and oval, bluish and purple, nonscaling areas of varying size distributed on the trunk and extremities. There were also bullous lesions, few and widely scattered, and edema of the penis and scrotum. There were no buccal lesions. The patient complained of intense pruritus and burning and of general malaise.

On Feb. 2, 1932, all the lesions were practically healed; no activity was present in any of them, but the affected areas were still clearly visible and recognizable by a circumscribed area of slight, brownish, almost café au lait pigmentation.

Examination of the urine on February 10 revealed no trace of phenolphthalein.

An almost circular patch of affected skin, about the size of a twenty-five cent piece, was removed surgically and lifted in toto from the flexor surface of the left forearm. A piece of healthy skin of the same size and shape was removed in the same manner from the extensor surface of the left forearm. The skin was ablated as for a full thickness graft, so that the epidermis and a good part of the cutis (not quite down to the subcutaneous fat) were contained in the graft. The affected skin from the flexor surface was carefully sutured into place in the defect on the extensor surface left by the removal of normal skin. The normal skin was sewed in a similar manner on the defect on the flexor surface which had previously been occupied by the excised patch. There were then present: (*a*) on the extensor surface of the forearm, a piece of previously affected skin in a heretofore unaffected area, and (*b*) on the flexor surface of the forearm, a piece of hitherto normal skin on a heretofore affected area.[13]

Under simple dressings both grafts were successful, the unaffected skin in toto, and the affected skin to the extent of about 65 per cent. A narrow margin at the periphery of the latter graft showed first some vesiculation and later a slight, superficial sloughing of the epidermis. The sutures were removed after one week,

13. Dr. Merlin W. Stone made the transplants.

and on March 29, 1932, healing was complete, both areas presenting flat, normal, nonpigmented, healthy-looking skin, with the exception of a narrow scar around the graft on the extensor surface, in the area in which sloughing had taken place. All the other areas were almost normal, there being no visible trace of the previous eruption, except slight pigmentation.

On March 29, 1932, at 2:30 p. m., a tablet containing 2 grains (0.12 Gm.) of phenolphthalein was given by mouth. Ten minutes later, intense pruritus and burning of the previously affected areas set in. There was no itching of the area on the extensor surface of the forearm to which the previously affected skin had been grafted. Within half an hour, all the previously affected areas became erythematous and edematous, and the patient's mouth and eyes, penis and scrotum became swollen. The erythema grew rapidly darker, and within an hour began to take on the dusky, purplish hue typical of this form of drug eruption. The area on the flexor surface of the forearm, now covered by heretofore normal skin, participated in the reaction, and became edematous, angry-looking and darker, in pace with the other areas. The area on the extensor surface of the forearm, now covered by the grafted heretofore affected skin, remained normal without subjective or objective change. The reaction of the various affected areas increased in severity during the next three days and then gradually subsided, leaving slight pigmentation. The

Fig. 1.—Phenolphthalein eruption. The photograph shows the left arm of A. L. (experiment 2). The affected patch, on the flexor surface, surrounded by a circle, was removed and transplanted to a site on the extensor surface of the forearm which had never participated in the eruption. A full thickness graft was employed. This section of skin, formerly reacting to phenolphthalein, when transplanted to the heretofore nonreacting site, remained normal after the ingestion of phenolphthalein.

graft area on the flexor surface of the forearm (heretofore normal skin on a formerly affected site) persisted in its reaction longer than the other areas, still being reddened and pigmented when the remainder of the skin had returned to normal. At no time during our observation did the graft of previously affected skin, occupying the heretofore normal area on the extensor surface of the forearm, show any subjective or objective change. (On April 7, 1932, the chemical examination for phenolphthalein demonstrated no traces of the drug in the urine.)

Conclusion.—After the ingestion of phenolphthalein in a typical case of fixed phenolphthalein eruption, the previously affected skin, grafted on and occupying a site which had not heretofore presented signs of hypersensitiveness remained normal. In contrast to this, a graft of heretofore normal skin did react, producing a typical lesion when grafted on a site previously hypersensitive. In other words, the previously affected area again reacted in spite of being covered by skin

transplanted from the normal area, and the previously normal area, in spite of being covered by the transplant of affected skin, remained normal.

In this experiment, then, the hypersensitiveness and immunity could not be proved to be situated either in the epidermis or in the superficial cutis, but seemed perhaps to be due to changes in the deeper tissues.

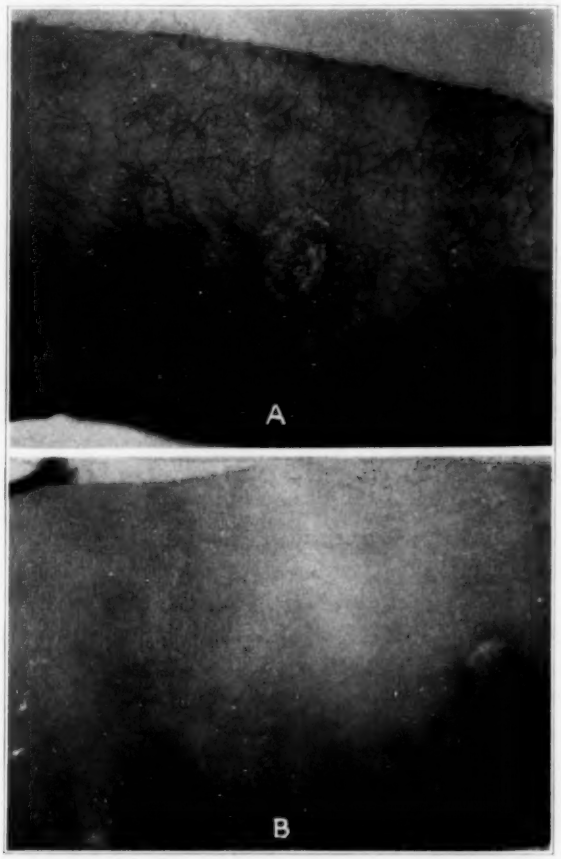

Fig. 2.—Phenolphthalein eruption. *A* shows the left forearm of A. L. and the graft of formerly affected skin occupying a hitherto normal site on the extensor surface of the forearm. This skin, although formerly participating in the reaction, now shows no reaction after the ingestion of phenolphthalein. The photograph was taken after the graft had healed and phenolphthalein had been administered. *B* shows the left forearm of A. L. and the graft of formerly unaffected skin occupying a hitherto affected site on the flexor surface of the forearm. This skin, although formerly not participating in the reaction, now shows the formation of a typical lesion after the ingestion of phenolphthalein. The photograph was taken at the same time as that in *A*.

The foregoing experiment, resulting in a phenomenon directly the opposite of what we had expected, merits further comment.

In an eczematous type of eruption (iodoform) and in hypersensitiveness to trichophytin, Bloch [14] was able to transfer the hypersensitiveness by means of skin grafts to other persons. But these grafts never took effect in a very satisfactory manner. The experiments have never been repeated, and Bloch himself later expressed the opinion that too much weight should not be placed on his results.

Naegeli, de Quervain and Stalder [15] performed an experiment identical with our experiment 2 in a case of fixed antipyrine eruption. They reported results diametrically opposed to ours. The previously affected skin reacted in its new site as it had before, and the normal skin transplant to the affected area remained without reaction. While it is true that they experimented with a different drug and that this may account for the difference in result, the fixed exanthems from antipyrine and from phenolphthalein seem so similar that this does not appear to be a satisfactory explanation. Further experiments of this nature are required, as the far-reaching significance of this question cannot be overestimated (for instance, for the understanding of the factors determining the localization of other skin diseases prone to recur in situ, like psoriasis, herpes and lupus erythematosus).

It is obvious that no generalizations may be made or definite conclusions drawn from two such isolated experiments as those of Naegeli and the one here described, performed under different conditions (a different drug, a different patient, varying intervals between the placing of the transplant and testing, unequal concentration of drugs, different thickness of the graft, different stages of the lesions when transplanted, etc.).

We have been prevented from repeating the experiment by the lack of further suitable cases. Fixed drug eruptions are in themselves rare, and nowadays most patients suffering from them are sufficiently enlightened to be able to ascertain the cause of the eruption by themselves, or have come to realize that the eruptions are harmless, and are, therefore, unwilling to submit to painful and unpleasant experimentation. (Naegeli, de Quervain and Stalder stated that they waited nine years before finding a suitable case.)

Just as the results of our transplantation experiment differed from those obtained in a case of fixed antipyrine eruption, our results of testing the skin in cases of phenolphthalein eruption do not correspond

14. Bloch, B.: Experimentellische Studien ueber das Wesen der Jodoform Idiosynkrasie, Ztschr. f. exper. Path. u. Therap. **9**:509, 1911.

15. Naegeli, de Quervain and Stalder: Cellulaerer Sitz der Allergie beim fixen Antipyrin Exanthem, Klin. Wchnschr. **9**:924, 1930.

to those reported by Apolant [16] in 1898, with positive reaction, in tests in which 10 per cent antipyrine ointment was used in a fixed antipyrine eruption. All that we have said concerning the different conditions of experimentation in the transplantations applies, in even greater degree, in the experiments with cutaneous tests.

We must limit ourselves to the statement that, as far as we have been able to determine by our experiments 1 and 2, no evidence could be brought forward which would prove the epidermis or superficial cutis to be the site of sensitivity of fixed phenolphthalein eruptions, under the conditions of our experiments and in the cases employed. Our results would point rather to the deeper tissues as the determinants of the localized reactions. The nerves and blood vessels terminating in the skin are the first possibilities which spring to one's mind. Unfortunately, little is known concerning the geographic figures formed by the end-branches of small nerve or blood vessel terminals in the skin. However, the oval and round shape of many fixed eruptions suggests the zones which might be supplied by the treelike branching terminations.

It was naturally of interest to attempt to find phenolphthalein in the body fluids in the cases examined, although we believe that such a demonstration of the presence of drugs is usually of little value in establishing a diagnosis. The situation is as follows: In cases of dermatoses in which the clinical aspect leads one to suspect a drug eruption, and in which the fact can be established that a drug has been taken, the demonstration of this drug in the urine, for instance, is of little aid. The drug, admittedly ingested by the patient, might be present for long periods even though its presence and ingestion had no relationship to the dermatosis. For example, a patient with hyperpigmentation following lichen planus or with bullous lesions in the mouth which were actually pemphigus would, if he were taking cathartics containing phenolphthalein, have this drug in his urine. Unfortunately, there is no evidence available which shows that patients with drug eruptions retain the responsible drug or excrete it in a different manner from normal persons or persons with other cutaneous diseases. The finding of drugs in the urine, even a long time after their ingestion, is, therefore, no proof that the eruptions under consideration are due to the drugs found. All that this demonstration proves is that the drug found has been taken at some time previously, and it is, therefore, of no value in cases in which this fact has already been ascertained. On the other hand, the finding of a suspected drug in the urine establishes the fact that it has been taken, and therefore

16. Apolant, H.: Die Antipyrin Exantheme, Arch. f. Dermat. u. Syph. **46**:345, 1898.

proves valuable in cases in which no other evidence of drug ingestion can be obtained. We shall give a short description of the method used for the demonstration of phenolphthalein in such cases.

The tissue was thoroughly dried and ground into fine particles. The total amount of tissue was divided into two parts. One part was extracted by ethyl alcohol in an extractor described by Myers and Wardell for blood cholesterol. The extract was evaporated to dryness on a steam bath and taken up in 80 per cent alcohol. Sodium hydroxide was added to this alcoholic solution to render it alkaline, and it was then acidified with acetic acid. The appearance of a pink color on the addition of the sodium hydroxide which disappeared after the addition of the acid was considered a positive, qualitative reaction for phenolphthalein.

The second portion of the tissue was suspended in normal hydrochloric acid to which pulverized zinc was added. The procedure was adopted to reduce any oxidized product of phenolphthalein. The mixture was then evaporated to dryness, transferred to the extractor and extracted with ethyl alcohol. The alcoholic extract was evaporated to a small volume, about 5 cc., and made alkaline with sodium hydroxide; a drop of blood was added, and from 3 to 5 drops of hydrogen dioxide. The appearance of a pink color which was dissipated by the addition of acetic acid was considered a positive reaction for phenolphthalein.

Analyses of urine were made in a similar manner. The urine was clarified by the addition of alcoholic zinc acetate in sufficient quantity to give a water-clear filtrate. The filtrate was evaporated to dryness, extracted and tested as for tissues.[17]

It is impossible to know how far the negative results of such tests can rule out the possibility of phenolphthalein having been taken. The following case illustrates the difficulty of this question:

Miss J. K., aged 40, was brought to us for consultation by Dr. J. J. Wiener. There was a history of an eruption identical with the one then present, which had appeared years previously and which had been diagnosed by Dr. Wiener as a phenolphthalein eruption. The patient had then admitted taking a cathartic containing this drug. After the original dermatosis had completely disappeared, Dr. Wiener had been able to reproduce it by giving the patient a phenolphthalein tablet. An eruption identical with the first one appeared almost immediately after this, and had had a similar course. The patient was warned against using laxatives containing phenolphthalein, and was told which of the popular patent preparations contain the drug. There is every reason to believe that the intelligent young woman followed instructions, as the eruption had been widespread, disfiguring and naturally of great annoyance to her. It incapacitated her in her profession, as there were lesions on her face, neck and hands. In spite of the averred strict adherence to instructions, the same form of dermatosis reappeared at irregular intervals during the next year and a half. The present attack, said to be the exact counterpart of previous eruptions, had occurred about one week before we were consulted. The patient, otherwise apparently in perfect health, presented an eruption of bluish-red and purplish circumscribed patches of varying sizes and shapes, disseminated over the trunk, hands, arms, face, neck, thighs and legs. The mucous membranes were not involved. The appearance of the eruption was that of a textbook case of

17. Professor John A. Killian, department of biochemistry, Post-Graduate Hospital, carried out these tests.

phenolphthalein eruption of the fixed circumscribed type. In spite of repeated lengthy periods of questioning, in which the patient gave evidence of an understanding of the situation and of every desire to cooperate and thus obtain relief, no history of the ingestion of a drug could be obtained (antipyrine, laxatives, sedatives, "cold or cough medicines" or "reducing" remedies). Examination of the patient's urine and of a piece of tissue removed for biopsy from an affected area on the right thigh proved negative for phenolphthalein.

As the patient recalled that she had had a drink of rye whisky and a glass of red wine on the day on which the eruption appeared, and could bring us samples of these, we performed tests to determine whether phenolphthalein had been used as coloring in either of the beverages. They gave negative results.

Notwithstanding all these negative findings, we are inclined to consider the eruption one of phenolphthalein dermatitis. We are led to this conclusion by the typical picture and by the previously established fact of hypersensitiveness to phenolphthalein demonstrating itself by an eruption identical with the one observed.

If this view is correct, it is necessary to explain two points which appear to contradict it. First, it is necessary to reconcile the negative tests for phenolphthalein in the urine and tissues. We do not believe that they are sufficiently conclusive to rule out the presence of small traces of the drug. These traces, so slight as to defy detection by even the finest chemical methods, are frequently found sufficient to cause severe and lasting results in hypersensitive subjects. (It is well known that immune biologic reactions in general are by far the most sensitive agents available for the detection and identification of infinitesimal traces of certain substances. This fact is made use of in legal medicine, for instance in order to detect the presence of human blood, semen, etc.) Consideration of the case of A. L. proves that unbelievably small quantities of phenolphthalein, traces certainly not capable of chemical demonstration, must suffice to cause some of these eruptions. When one considers the relatively small dose (2 grains [0.12 Gm.] for a man weighing over 200 pounds [90 Kg.]), the poor solubility of the drug and its high dilution in the body fluids before reaching the skin, together with the speed with which the reaction began to appear in this case (onset within ten minutes after the placing of the tablet in the mouth), one no longer doubts that eruptions may be caused by such incredibly infinitesimal amounts that strictly chemical methods must fail to discover the drug. (Attention is directed to the fact that, in spite of our definite knowledge that phenolphthalein had been taken by A. L., the most careful chemical investigations of the urine repeatedly gave negative results a few days after the ingestion of the drug. These small amounts as causes of reactions make one think of the

possibility that the reactions may be caused, not by the drugs themselves, but by traces of accompanying impurities not demonstrable chemically.)

The second point which must be explained in the case of Miss J. K. is the question of how the patient had come into contact with phenolphthalein. We believe that her story was reliable and that she was not conscious of having taken the drug in any form. We therefore began to look for vehicles other than the usual laxatives in which phenolphthalein is embodied. The whisky and wine examined showed no trace. A further investigation showed that there must be added to the list of the usual well known preparations, the following: (1) certain mouth washes and lotions of a pink or reddish color; (2) most sodium perborate (aromatized) preparations for use in the mouth and for douches; (3) possibly some tooth pastes, and (4) even the pink icing which decorates certain cakes. On this last discovery (Dr. E. W. Abramowitz [17a] called our attention to the presence of the drug in cakes), it became apparent that the possibility of contact with phenolphthalein cannot be definitely excluded in any case. We believe that the appearance of the eruption within from ten to fifteen minutes after the taking of a laxative tablet (as we have seen occur several times, and as reported in experiment 2) shows that phenolphthalein eruptions may possibly be caused by mouth washes, tooth cleansers and similar preparations. It is conceivable that the drug may even be absorbed through the mucous membrane of the mouth, and small amounts of mouth wash are inevitably swallowed by those who employ it. Absorption through the mouth may be aided because phenolphthalein is more soluble in alkaline than in acid mediums, and the mouth is usually more alkaline than the stomach.

In any case the speed of absorption speaks in favor of penetration of the drug through the parts of the digestive tract superior to the pylorus.

Since in vitro methods of chemical demonstration were shown to be far from infallible, we decided to attempt a demonstration of phenolphthalein in vivo within the affected tissues. We tried to do this by means of the technic described in experiment 3.

EXPERIMENT 3.—In a case of proved fixed phenolphthalein eruption, we forced hydrogen and hydroxyl ions into the skin of the affected areas by means of cataphoresis. For this purpose tenth-normal hydrochloric acid solution and tenth-normal solution of sodium hydroxide were employed. With the accepted technic we moistened the anode with the hydrochloric acid solution and applied it to an area of purplish hue with a current of 2 milliamperes for about half an hour. No change in color followed this procedure beyond a slight erythema, which was

17a. Abramowitz, E. W.: Phenolphthalein Eruptions Produced by the Eating of Iced Cup Cakes, M. J. & Rec. **136**:31 (July 6) 1932.

evidently due to the irritating effect of the electrical current, and which lasted about half an hour. The results were the same when the cathode was moistened with the sodium hydroxide solution. The lesions were observed during several days and did not evidence any change due to cataphoresis beyond a few superficial, pinhead-sized crusts where small burns had presumably occurred. There was neither paling nor change in hue.

Conclusion.—Cataphoresis of hydrogen ions (acid) and of hydroxyl ions (alkaline) did not cause purplish phenolphthalein lesions to change color. (Phenolphthalein is, of course, an indicator, becoming red in an alkaline medium; its demonstration could have been considered as successful provided the lesions had taken on a more pinkish or reddish tone after the application of the sodium hydroxide solution or had lost some of their red tinge after cataphoresis with the hydrochloric acid solution.)

We were unsuccessful in our attempt to demonstrate phenolphthalein in vivo by this method. (To our knowledge there is no eminently satisfactory explanation for the peculiar purplish and brownish-blue color of many phenolphthalein and antipyrine eruptions. The brownish tinge which they present on healing may be due to pigments of autochthonous type, such as melanin or hemosiderin. Wise and Abramowitz [18] reported that the granules did not give iron reactions with Perls' method, and concluded that the pigment was melanin.)

The last experiment concludes those which we wish to report on fixed phenolphthalein eruptions, and we now turn to several clinical observations. Before speaking of some of the rarer forms of phenolphthalein hypersensitiveness, we again call attention to a fact mentioned in the reports of experimentation, namely, the many opportunities for ingestion of the drug in forms other than the proprietary laxatives, and the resultant practical impossibility of absolutely ruling out this drug by taking the most careful history. We now include in our questions and our interdictions to patients all pink mouth washes and tooth pastes, all foods colored pink in which the coloring matter might be due to phenolphthalein dyes and all proprietary perborates and similar substances. Perhaps some of the cases in which apparently reliable and intelligent patients deny all contact with phenolphthalein laxatives and yet have recurrences of apparently typical eruptions may be caused by such preparations. (Of course, theoretically, other drugs or toxins can cause eruptions of this type.)

We shall be brief regarding the rarer clinical pictures we report. Within the last year we have seen two cases of subungual, bluish-purplish, sharply demarcated changes of color affecting the proximal portion of the nail bed of all the fingers. These, at first glance, looked somewhat

18. Wise, F., and Abramowitz, E. W.: Phenolphthalein Eruptions, Arch. Dermat. & Syph. **5**:297 (March) 1922.

like bruised or hemorrhagic areas, but on closer inspection they resembled what phenolphthalein areas may be supposed to look like when viewed through the nail plate. There were no other phenolphthalein lesions present. Even the toe-nails appeared unaffected.

The first case was that of a young man, a patient of Dr. Benjamin Ochs, who brought the patient to the Post-Graduate Hospital Skin Clinic. We saw this patient shortly after the appearance of Campbell's [19] article on ungual changes due to phenolphthalein. Campbell did not prove that the changes in the nails in his case were due to phenolphthalein by attempting to cause a reappearance of the condition by readministering the drug. Ochs' case is therefore the first in which such proof has been brought, as in this patient the clinical test proved successful.

A few weeks later we saw a second case essentially identical with Dr. Ochs', in a middle aged woman. In this case we could follow the course of the disease; the nail beds and perionychial tissues became tender and discolored and resembled chronic low grade paronychias, and the nails grew deformed, with heaped up transverse ridges such as one sees resulting from an eczematous process of the nail matrix.

Sensory disturbances of the tongue and mouth are another unusual manifestation which we believe may be caused by phenolphthalein in some cases. They are similar to the paresthesias described by Lain [20] as a result of electrical currents in the mouth. There are burning and tingling, often very persistent and maddening, without visible changes in the mucosa. (Sometimes we thought that we saw a slight increase in redness, but if this was so, it was so little marked that it may have been due to friction for relief. It in no way resembled typical phenolphthalein lesions in the mouth.) We have seen three cases which we believe we are justified in putting into this category (there were a history of taking phenolphthalein and relief when on our advice this drug was discontinued, and there was no other demonstrable cause for the paresthesias).

SUMMARY AND CONCLUSIONS

In this paper the term drug eruptions is used to report eruptions of all kinds caused by medicaments. While knowledge concerning the mechanisms of sensitization in eczematous and urticarial types of eruption has been decidedly advanced in recent years, this is not the case in eruptions of the fixed type. Phenolphthalein eruptions are excellent examples of this form, and offer the American dermatologist material for investigation.

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19. Campbell, G. Gordon: Unusual Pigmentation of the Nails from Phenolphthalein, Brit. J. Dermat. **43**:186, 1931.

20. Lain, Everett S.: Chemical and Electrolytic Lesions of the Mouth Caused by Artificial Dentures, Arch. Dermat. & Syph. **25**:21 (Jan.) 1932.

In the first experimental study we attempted to bring light on the question of the exact seat of hypersensitiveness in fixed phenolphthalein eruptions, more particularly to ascertain whether the epidermis or superficial cutis or both are the sensitive or shock tissue. Cutaneous tests performed on both affected and unaffected sites in patients with fixed phenolphthalein lesions and on normal controls did not reveal any definitely demonstrable hypersensitiveness of the skin in patients with eruptions due to phenolphthalein. The patch test reactions and the immediate wheal reactions were as in normal persons, whereas the later papular reaction to intradermal tests seemed slightly increased in the cases of drug eruption, but not sufficiently to allow definite conclusions in the small series available (three cases of phenolphthalein eruption and five controls).

In our second experiment, the problem was approached from a different angle, namely, by autogenous transplantations of skin of full thickness. An affected area was transplanted to a normal site, and normal skin was transplanted to an affected site. After complete healing, phenolphthalein was administered by mouth. Contrary to our expectations, and to the results reported by Naegeli and his collaborators, (*a*) the normal skin grafted on the previously affected area reacted in a typical manner, with the production of a phenolphthalein lesion, while (*b*) the previously affected skin, now grafted on a heretofore normal site, remained unaffected.

The experiments bring no proof that the epidermis or superficial cutis (or both) is the "shock site" and seem rather to favor a theory of regional hypersensitiveness, dependent on deeper structures (nerves, blood vessels).

A method for the demonstration of phenolphthalein in tissues and body fluids is described. This method, which is one of the most sensitive in vitro methods available for this purpose, failed to disclose phenolphthalein in the urine and affected tissue of a patient known to be sensitive to the drug and having a typical phenolphthalein eruption. This may be explained by the fact that immune-biologic reactions are frequently more sensitive than any chemical laboratory test.

We call attention to the possibility that phenolphthalein may be ingested in many ways besides in the well known laxative preparations (pink mouth washes, tooth pastes, sodium perborate preparations and even icings on cakes may contain traces of the drug, and these traces alone may be sufficient to cause an eruption in highly sensitive subjects).

In view of the relative uncertainty of in vitro methods, an attempt was made to demonstrate phenolphthalein in affected areas in vivo. This was unsuccessful, as cataphoresis of acid and alkaline ions failed to produce any change in the color of the lesions which could be ascribed to an indicator action.

Attention is called to apparently rarer manifestations of phenolphthalein idiosyncrasy, the first being subungual and periungual lesions without other involvement of the skin and mucosae, and the second, paresthesias of the tongue and buccal mucosae in the absence of visible lesions. In a case in which the nails were affected the etiology was proved by the ingestion test; in the other cases the decision as to etiology was founded on clinical evidence alone.

DISCUSSION

Dr. George M. MacKee, New York: The authors have demonstrated by cutaneous tests and by the surgical transfer of an area of skin that in one case of phenolphthalein eruption the sensitivity was in the subcutaneous tissue rather than in the skin. In my opinion, based on their work, personal experience and reports in the literature, it is probable that in some cases the sensitivity is in the subcutaneous tissue while in others it is in the skin. This fact may account for phenolphthalein eruptions of different types, such as eczema or erythema.

The authors mentioned delayed eruptions following the application of butesin picrate to sensitized persons. In one case of a burn to which the ointment had been applied, sensitization occurred only where the chemical was in contact with the skin. The burn healed rapidly. The eruption affected the surrounding skin, but not the new skin. Later, however, the newly formed skin also became sensitized. These delayed reactions are probably analogous to the delayed reactions seen in patch tests and other conventional cutaneous tests, and they alter the mode of approach in determining the causative factor in cases of dermatitis venenata. In other words, one must ascertain every substance that has come in contact with the skin on the day preceding the eruption, and every day for a week before the eruption appeared.

The test that Drs. Wise and Sulzberger made with cataphoresis is not convincing, because it remains to be proved whether or not the drug can be carried into the skin by an electric current.

Dr. Walter J. Highman, New York: The significance of these experiments transcends the authors' immediate conclusions, indicating how one may begin to explain the moot question as to localization that has been engaging attention for so long. In these studies it was the site and not the particular piece of skin that seemed to determine the lesion.

There are two factors to be considered in the localization of lesions: the anatomic site of the tissue that reacts to the toxin, and also some local property in the tissue, which must be universal, which makes it possible for the tissue to react. Dr. Wise and Dr. Sulzberger have given the first real light as to why lesions localize themselves at particular places. I think this is just as significant as any of the many pregnant points that have been brought out. I consider this a remarkable contribution to medicine and worthy of substantiation.

Dr. Fred Wise, New York: With reference to Dr. MacKee's remarks, he is right about our not proving that we performed cataphoresis, although our technic was correct, and he is justified in saying that this should be definitely proved. It was an experiment which should be repeated.

Dr. Highman flattered us in his discussion. In Naegeli's clinic the workers experimented with an antipyrine fixed eruption which is almost indistinguishable from some of the phenolphthalein eruptions, and their results were the opposite of ours with respect to the tissue transposition tests. We have not yet had oppor-

tunities to do a sufficient amount of experimental work, for it is difficult to find many patients with phenolphthalein eruptions who will allow us to carry out operative transference experiments. Naegeli and his co-workers waited nine years before they obtained a suitable patient for this purpose.

We performed a full thickness skin graft, while Naegeli used an epidermal graft. Bloch performed a similar experiment by transposing a graft to another patient. He says that his results were not satisfactory and should not be taken into consideration from the standpoint of definite scientific conclusions, for his grafts did not "take" well. However, the full thickness grafts that we made "took" fairly well.

EFFECT OF MENSTRUATION ON THE INCIDENCE OF DEMENTIA PARALYTICA

RUDOLPH HECHT, B.S., M.S.
CHICAGO

It has long been recognized that some persons are more susceptible to certain diseases than others. Some of the causes are well recognized, such as racial or constitutional ones; others are obscure and uncertain. It seems fairly definite that sexual factors play a part in the incidence of several diseases.

It is thought with good reason that the menstrual function is concerned in this difference in susceptibility. It is said to be the factor which excites many latent appendical infections. Some of the dermatoses, such as acne, are worse during the menstrual cycle. Instances of hypertension at each premenstruum have been reported. Lapinsky [1] has reported increased dermographism with each menstrual period; a phenomenon even more striking is the peculiar susceptibility of the young female to tuberculosis. In all of these, biologic effects of the menstrual cycle are not unlike those following nonspecific protein therapy.

Most syphilologists agree that nonspecific protein therapy is of decided influence in syphilis, both early and late.[2] The beneficial effects are thought to be due to the shock reaction. There is disagreement as to what element in the reaction or what phase of the reaction is responsible for the favorable results. Wagner von Jauregg [3] considers the fever the important factor. Fever, of course, may inactivate or destroy the spirochete, which is very susceptible to slight variations in temperature. Sherber [4] and Kundratitz [5] expressed the belief that the spiro-

From the Department of Pathology and Bacteriology, University of Illinois College of Medicine.

1. Lapinsky, M.: Ztschr. f. d. ges. Neurol. u. Psychiat. **22**:58, 1914.

2. (*a*) Bering, F.: Wien. klin. Wchnschr. **41**:977, 1928. (*b*) Memmesheimer, A. M.: Arch. f. Dermat. u. Syph. **156**:500, 1928. (*c*) Weirauk, H. V.: Ohio State M. J. **22**:305, 1926. (*d*) Herrold, R. D.: Protein as an Adjunct in Treatment of Resistant Syphilis, J. A. M. A. **86**:413 (Feb. 6) 1926. (*e*) Kerl, W.: Arch. f. Dermat. u. Syph. **157**:294, 1929. (*f*) Finger, E.: Wien. klin. Wchnschr. **41**:771, 1928. (*g*) Greenbaum, S. S., and Wright, C. S.: Value of Nonspecific Protein Therapy in Syphilis, Arch. Dermat. & Syph. **12**:858 (Dec.) 1925. (*h*) Engman, M. F.; Jorstad, L. H., and Engman, M. F., Jr.: Experimental Study of Early Syphilis with Nonspecific Therapies, J. A. M. A. **97**:1503 (Nov. 21) 1931.

3. von Jauregg, Wagner: Psychiat.-neurol. Wchnschr. **19**:20, 132 and 251, 1918; Wien. med. Wchnschr. **59**:2124, 1909; Jahrb. f. Psychiat. u. Neurol. **7**:94, 1887.

4. Sherber, G.: Wien. klin. Wchnschr. **39**:1325, 1926.

5. Kundratitz, K.: Monatschr. f. Kinderh. **37**:501, 1927.

chetes were mobilized into the blood stream after the injection of foreign protein, and then that the defense mechanisms of the body achieved their destruction. There are two phases to this reaction. Phase 1 was characterized by a fever, and phase 2, by a reaction after the fever and a return to normal. Leukocytosis with a myeloid tendency has been demonstrated.[6] Petersen [7] has studied the serum ferments. An increase in fibrinogen has been shown.[8] Jobling and Petersen [9] demonstrated an increase in the proteolytic enzymes. Eggstein [10] has shown acidosis. Changes in the metabolic rate and the permeability have been studied,[11] and Müller and Petersen [12] have shown a dominance of the sympathetic. Hoff [13] summarizes the important changes which occur as follows:

PHASE 1

1. Beginning and maintenance of fever
2. Leukocytosis with a myelogenous tendency
3. Lowering of the alkali reserve
4. Increase of metabolism
5. Increased destruction of protein
6. Increase in the blood sugar
7. Lowering of the blood cholesterol
8. Dominance of the sympathetic

PHASE 2

1. Decline of the fever
2. Decrease of the leukocytes with a lymphatic tendency
3. Rise of the alkali reserve
4. Decreased metabolism
5. Lowered destruction of protein
6. Decrease in the blood sugar
7. Rise of blood cholesterol
8. Dominance of the parasympathetic

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6. Jobling, J. W.: Nonspecific Substances, Arch. Int. Med. **19**:1402 (June) 1917. Scully, F. T.: Reaction After Intravenous Injections of Foreign Protein, J. A. M. A. **69**:20 (July 7) 1917. Müller, E. F.: Ztschr. f. d. ges. exper. Med. **32**:120, 1923. Cowie, D. M., and Calhoun, H.: Nonspecific Therapy in Arthritis and Infections, Arch. Int. Med. **29**:69 (Jan.) 1919.

7. Petersen, W. F.: Ferment-Antiferment Balance, Arch. Int. Med. **20**:515 (Oct.) 1917; Protein Shock Therapy, ibid. **20**:716 (Nov.) 1917; Resistance to Tuberculosis, ibid. **21**:14 (Jan.) 1918; The Nonspecific Reaction, J. A. M. A. **76**:312 (Jan. 29) 1920.

8. Löwy, J.: Zentralbl. f. inn. Med. **37**:833, 1916.

9. Jobling, J. W., and Petersen, W. F.: Bacteriotherapy in Typhoid Fever, J. A. M. A. **65**:515 (Aug. 7) 1915.

10. Eggstein, A. A.: J. Lab. & Clin. Med. **6**:481, 1921.

11. (*a*) Barr, D. P.; Cecil, R. L., and DuBois, E. F.: Clinical Calorimetry, Arch. Int. Med. **29**:608 (May) 1922. (*b*) Petersen, W. F.: Protein Therapy, New York, The Macmillan Company, 1922.

12. Müller, E. F., and Petersen, W. F.: Klin. Wchnschr. **5**:53, 1926.

13. Hoff, H.: Unspezifische Therapie, Berlin, Julius Springer, 1930.

Of special significance is the leukocytosis with the "shift to the left." Not only are defensive mechanisms of this type stimulated, but, according to some investigators, there is a concomitant rise of all the immune bodies.[14] It is reasonable to believe that in the presence of a syphilitic infection, the stimulation to the production of all the immune bodies would also stimulate the production of the antibodies for syphilis. Not only does the injection of protein have this nonspecific effect, but mercury also is said to exert its action in a like manner. The concentration of mercury, whether attained by ingestion, injection or inunction, is insufficient to destroy the spirochete; however, Bergel[15] has shown that mercury acts on the lymphocytes about the spirochetes, destroying the lymphocytes and liberating their enzymes. The effect of the mercury is thought to last only as long as lymphocytes are present.

With the knowledge that these reactions can be produced artificially, the question arises: Do such "shock reactions" ever occur in a person without the introduction of foreign protein? Such reactions undoubtedly do occur, for when a person has an acute febrile disease he experiences the same reactions as does one who receives a protein shock. There are innumerable clinical observations to substantiate this statement. Beneficial effects have been noted when fever or trauma is superimposed on certain conditions, especially the psychoses or organic diseases of the brain.[16] Savage[17] reported the beneficial effect of a carbuncle in a case of dementia paralytica. Psychiatrists have long known that erysipelas occurring in a patient with dementia paralytica may be of great benefit. Menninger-Lerchenthal[18] discussed various neurologic conditions in which the patient has been aided by intercurrent infections. Furthermore, patients having such diseases as lupus,

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14. Rumpf, T.: Deutsche med. Wchnschr. **19**:987, 1893. Hektoen, L.: Vaccine Therapy, J. A. M. A. **66**:1591 (May 20) 1916; Precipitin Production in Allergic Rabbits, J. Infect. Dis. **21**:279 (Sept.) 1917. Pfeiffer, R.: Ztschr. f. Hyg. **16**:268, 1894. Weichardt, W.: München. med. Wchnschr. **66**:289, 1919; **67**:91 and 1085, 1920; **68**:365, 1921. Buchner, H.: München. med. Wchnschr. **38**:841, 1891. Flechseder, R.: Wien. klin. Wchnschr. **29**:637, 1916.

15. Bergel, S.: Klin. Wchnschr. **1**:204, 1922.

16. (*a*) Mayberry, C. B.: J. Nerv. & Ment. Dis. **19**:298, 1894. (*b*) Beckmann, J.: Diss., Kiel, 1914; abstr., Neurol. Centralbl. **35**:316, 1916. (*c*) Hessler, R.: Epilepsy and Erysipelas, J. A. M. A. **30**:1157 (May 14) 1898. (*d*) Azemar, C.: Neurol. Centralbl. **21**:918, 1902. (*e*) Dobrschansky, M.: Neurol. Centralbl. **26**:824, 1907. (*f*) Parhon and Urechie, quoted by Donath, J.: Ztschr. f. d. ges. Neurol. u. Psychiat. **19**:223, 1913. (*g*) Hamilton, A. S.: Effect of Intercurrent Disorder on Pre-Existing Epilepsy, J. A. M. A. **53**:1902 (Dec. 4) 1909. (*h*) Wachsmuth: Psychiat.-neurol. Wchnschr. **27**:239, 1925. (*i*) Werner, cited by Menninger-Lerchenthal, E.: Allg. Ztschr. f. Psychiat. **90**:359, 1929. (*j*) Bach, C.: Neurol. Centralbl. **16**:186, 1897. (*k*) Herschmann, H.: Wien. klin. Wchnschr. **27**:1404, 1914.

17. Savage, quoted by Menninger-Lerchenthal.[16i]

18. Menninger-Lerchenthal.[16i]

asthma, malignant growths and a host of others have been reported improved or even cured by intercurrent infections.[19]

Of late years, however, more and more evidence has accumulated to show that not only at the time of a severe, acute infectious disease or following an injection of protein does a person undergo a "shock reaction," but that even during so-called normalcy certain closely related physiologic fluctuations occur. This is true especially in the female.

Our methods of nonspecific stimulation are indeed crude when compared to the finely adjusted and regulated mechanisms of nonspecific resistance used by the living organism to ward off contagion and disease. An example of such a mechanism is the secretion of a highly acid eccrine sweat as shown by Marchionini [20] and others, which exerts a protective influence on the surface of the skin, preventing infection. This self-sterilizing power of the skin has been thoroughly investigated by Arnold,[21] Cornbleet [22] and their associates.

Not only does the skin possess nonspecific powers of resistance, but even in the normal physiologic reactions of the body, especially during the menstrual cycle, there seems to be a protective power far greater than heretofore supposed. Petersen [23] has shown the tremendous swings and alterations in the reactivity of the female during the menstrual cycle. In his study of the changes incident to the menstrual cycle in normal and diseased patients, he divides the changes into those of the premenstrual and postmenstrual periods. He has summarized the most important changes of the premenstruum as follows:

1. Increased capillary permeability
2. Relative increase in acidity
3. Reduction of intermediary oxidation
4. Decrease in carbon dioxide content
5. Increase of the blood and tissue chlorides with fluid retention
6. Decrease in cholesterol
7. Increase in the activity of proteolytic and lipolytic enzymes
8. Increase in hormone activity
9. Autonomic instability

He stated that in the postmenstruum opposite changes occur.

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19. Petersen, W. F., in Jordan, E. O., and Falk, I.: The Newer Knowledge of Immunity, Chicago, University of Chicago Press, 1928, p. 1086; footnote 11*b*. Hoff.[13]

20. Marchionini, A.: Arch. f. Dermat. u. Syph. **158**:290, 1929; **154**:690, 1928; Klin. Wchnschr. **8**:924, 1929; **7**:12, 1928.

21. Arnold, L.; Gustafson, C. J.; Hull, T. G.; Montgomery, B. F., and Singer, C.: Am. J. Hyg. **11**:345, 1930. Arnold, L., and Singer, C.: Proc. Soc. Exper. Biol. & Med. **27**:364, 1930.

22. Cornbleet, T., and Montgomery, B. E.: Sterilizing Powers of the Skin, Arch. Dermat. & Syph. **23**:908 (May) 1931.

23. Petersen, W. F., and Hecht, R.: Contrary Therapeutic and Sex Relationship of Syphilis and Tuberculosis, J. A. M. A. **99**:108 (July 9) 1932.

Menninger-Lerchenthal [18] stated: ". . . the increase in the blood iodides, the increase in the lipoid content of the blood and the changes in the vegetative nervous system and in the chemistry of the body fluids are all proof of the deep effect of the menstrual changes in the female."

Thus, at each menstrual period the female undergoes an upheaval and adjustment comparable in many respects to that following protein therapy or infection, and consequently a woman with syphilis will experience each month a nonspecific shock reaction, which may act to prevent the development of neurosyphilis in later life. The most satisfactory results with nonspecific protein therapy have been obtained in the treatment of neurosyphilis, especially dementia paralytica. Mattauschek and Pilcz [24] stated that syphilitic patients who have had an acute infection since the onset of the syphilis are protected against later dementia paralytica, and Bering [2a] stated that malaria therapy when used in early syphilis is a prophylactic against subsequent neurosyphilis.

It is known that dementia paralytica is less common in females than in males. My associates and I undertook a statistical study to verify this, and we came to the conclusion that apparently throughout the world the incidence of dementia paralytica in males as compared to females is about three males to one female.[25]

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24. Mattauschek, E., and Pilcz, A.: Ztschr. f. d. ges. Neurol. u. Psychiat. **15**:608, 1913; **8**:133, 1912.

25. (*a*) Obersteiner, H.: Die progressive allgemeine Paralyse, Vienna, Hölder-Pichler-Tempsky A.-G., 1908. (*b*) Moore, J. H.: Studies in Asymptomatic Neurosyphilis, Arch. Int. Med. **30**:548 (Nov.) 1922. (*c*) White, W. A.: Outlines of Psychiatry, Washington, D. C., Nervous and Mental Disease Publishing Company, 1926. (*d*) Stokes, J. S.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1927. (*e*) Dana, C. L.: Text Book of Nervous Diseases, New York, William Wood & Company, 1925. (*f*) Mettler, L. H.: A Treatise on Diseases of the Nervous System, Chicago, Cleveland Press, 1905. (*g*) Kellogg, T. H.: Text Book of Mental Diseases, New York, William Wood & Company, 1897. (*h*) Church, A., and Peterson, F.: Nervous and Mental Diseases, Philadelphia, W. B. Saunders Company, 1903. (*i*) Brower, D. R., and Bannister, H. M.: A Practical Manual of Insanity, Philadelphia, W. B. Saunders Company, 1902. (*j*) Pearce, F. S.: A Practical Treatise on Nervous Diseases, New York, D. Appleton and Company, 1904. (*k*) Stoddart, W. H. B.: Mind and Its Disorders, Philadelphia, P. Blakiston's Son and Co., 1922. (*l*) Defendorf, A. R.: Clinical Psychiatry, New York, The Macmillan Company, 1902. (*m*) DeFursac, J. R., and Rosanoff, A. J.: Manual of Psychiatry, New York, John Wiley & Sons, 1908. Mendel, E.: Die progressive Paralyse der Irren, Berlin, A. Hirschwald, 1880.

The next problem which presents itself is: What is the incidence of syphilis in males as compared to females? This is difficult to determine, but, as I shall show later, I believe that we have been able to surmount the greatest difficulty by means of certain statistical studies made at the Cook County Hospital in Chicago.[26] The published figures for the incidence of syphilis in males and females are so variable that little can be gained by a study of them.

It has been said that there are fewer females with syphilis than males, and therefore that the incidence of dementia paralytica should be less among females. Possibly females are just as liable to infection as are males, but are better able to suppress or dispose of the infection having once acquired it. The demonstration of the primary lesion in the female is often difficult, and is frequently unnoticed, while in the male this is rarely the case. Thus the male should apply for diagnosis and treatment more frequently than the female, and consequently swell the statistics of the incidence of early syphilis in males. If the Wassermann or Kahn test is applied as a routine, does this difference in the two sexes still hold?

There is no doubt that females who have acquired syphilis are, as Pusey[27] says, ". . . better able to handle it" than males. Moore[25b] stated the belief that this difference is due to child bearing on the part of the female, and quoted statistics from the Johns Hopkins Hospital to prove his contention. My associates and I believe that the phenomenon which is responsible for this immunity is one which is more fundamental than pregnancy. In the nineteenth century Lunier and Baillarger[28] suggested that fewer females had dementia paralytica than males because of menstruation, and in the light of Petersen's recent work, we believe that there is proof that if the menstrual cycle is not the most important factor in this immunity, at least it is very significant. As a further proof, dementia paralytica in the female is said to be equal to that in the male following the menopause (when the protective influence of menstruation is lost).[29]

The explanation of the beneficial effects of the menstrual cycle probably lies in the nonspecific changes of the premenstrua, which have been discussed. Thus, in an infection like syphilis this process probably has a lytic effect on the storehouses of the spirochetes and unwittingly gives the female ideal treatment, namely, the mobilization of the organisms and their consequent destruction by the activated or stimulated defense mechanisms.

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26. The records of the Cook County Hospital were obtained through Dr. R. H. Jaffé.

27. Pusey, W. A.: Personal communication.

28. Lunier and Baillarger, quoted by Obersteiner.[25a]

29. Defendorf.[25l] DeFursac and Rosanoff.[25m] Lunier and Baillarger.[28]

In order to lend support to this belief, we investigated the records of Wassermann and Kahn reactions of the blood at the Cook County Hospital to note the relative incidence of positive reactions in males and females. Records were studied for the years 1929 to 1931, and

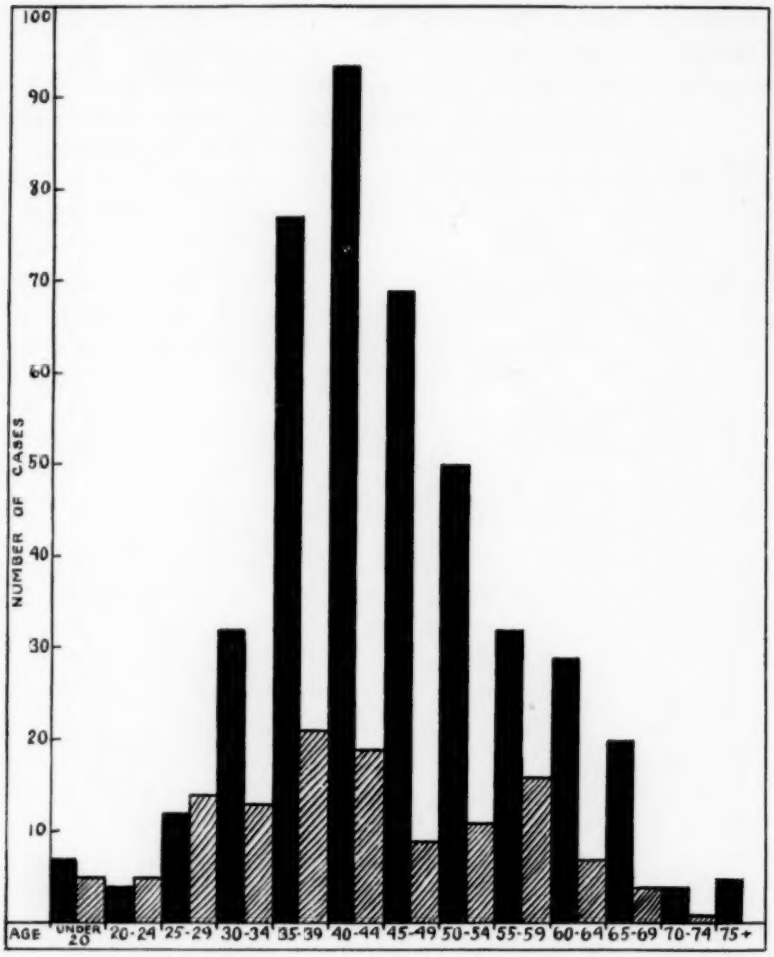


Chart 1.—A graph showing the incidence of dementia paralytica in males and females at the Cook County Hospital in Chicago for the years 1925 to 1931 inclusive. The solid black columns represent males, those with diagonal lines, females. The ratio is three males to one female with dementia paralytica. Further, it shows the second rise in the incidence in females following the menopause, that is, age group 55 to 59.

represent the reactions in a mixed population in which, we believe, the females were just as liable to infection as were the males.

Of 49,852 patients on whom Wassermann or Kahn tests were performed in the three years, 24,290 were males and 25,562 were females. For the total of the three years a positive reaction was obtained in

TABLE 1.—*Relative Incidence of Positive Reactions in the Two Sexes*

	Year			
	1929	1930	1931	Total
Total Wassermann	14,917	17,683	17,252	49,852
Total males negative	6,381	6,764	7,027	20,172
Total females negative	5,969	7,867	7,363	21,199
Total males positive	1,328	1,446	1,344	4,118
Total females positive	1,239	1,606	1,516	4,363
Total males and females negative	12,350	14,631	14,390	41,371
Total males and females positive	2,567	3,952	2,862	8,481
Total males +++, ++++	755	564	411	1,730
Total females +++, ++++	664	622	492	1,778
Total males ±, +, ++	573	862	933	2,368
Total females ±, +, ++	575	985	1,026	2,585
Percentage males positive	17.23	17.61	16.05	16.96
Percentage females positive	17.19	16.95	17.09	17.08
Percentage males +++, ++++	9.79	6.90	4.90	7.19
Percentage females +++, ++++	9.21	6.57	5.54	7.11
Percentage males ±, +, ++	7.43	10.74	11.15	9.77
Percentage females ±, +, ++	7.98	10.39	11.55	9.97

TABLE 2.—*Comparison of Age Groups in General Population in Cook County Compared with Age Groups of Patients with Dementia Paralytica in Cook County Hospital*

	Population		Dementia Paralytica	
Age Groups	Male	Female	Male	Female
Under 20	290,564	689,842	9	5
20 to 24	181,283	196,031	2	5
25 to 29	189,457	191,633	12	14
30 to 34	182,671	179,491	33	13
35 to 44	358,940	325,084	171	40
45 to 54	235,519	205,176	118	20
55 to 64	126,928	122,393	61	23
65 to 74	60,494	63,426	24	5
75	16,392	21,725	5	0
Unknown	2,749	1,907	6	1
Total	2,044,997	1,996,708	441	126

16.96 per cent of the males and 17.08 per cent of the females. Reactions of plus three and plus four were obtained in 7.19 per cent of the males as compared to 7.11 per cent of the females. The male plus or minus, plus one and plus two reactions were 9.77 per cent, as

compared to 9.97 per cent in the females. Thus at the Cook County Hospital the incidence of positive Wassermann or Kahn tests of the blood in females slightly exceeds the figures for males.

We next investigated the number of male and female patients with dementia paralytica at the Cook County Hospital. Records were available for the years 1925 to 1931. These confirmed the incidence which

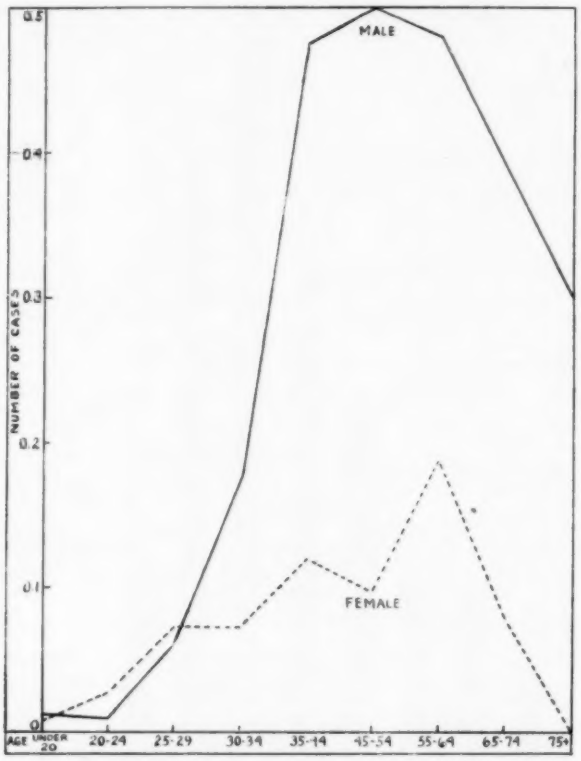


Chart 2.—This is a graph showing the incidence of dementia paralytica in males compared to that in females at Cook County Hospital in Chicago per thousand male and female population, according to the United States Census figures of population in Cook County for 1930. Here again a visual picture is presented of the greater number of males affected than females in the various age groups in relation to the number of males and females alive in these various groups. Note the rise in the number of females at the time of the menopause, when the female has lost the protective powers of the menstrual cycle. The curve for males reaches its height at about 35 years, while the curve for females does not do so until 55 years, the latter age coinciding with the time of the menopause.

was noted by most authorities throughout the world, there being approximately three males to one female with dementia paralytica. It

has been said that when a man becomes incapacitated, the family income is shut off and he has to enter a charity hospital; but if, for example, dementia paralytica develops in his wife, he can afford private care of her, and that this is in part responsible for the high incidence of males in public practice. I doubt whether this is entirely true, since figures throughout the world seem to be about the same. Further, Dana,[25e] for example, stated that in private practice there are ten males with dementia paralytica to one female.

For the years 1925 to 1931 there were 441 males as compared to 126 females with dementia paralytica at the Cook County Hospital, giving a ratio of 3.5 males to 1 female.

Table 2 shows the various male and female age groups in the population of Cook County according to the 1930 census, compared to the various male and female age groups of patients with dementia paralytica at Cook County Hospital for the years 1925 to 1931, inclusive.

Objections can be raised to using the population of the whole county as a comparison to a small group as at the County Hospital, yet we believe that this is possible as a means of demonstrating the fact that although the various age groups of the population are practically alike for males and females, the incidence of dementia paralytica varies in the male and female. We also believe that these figures can be used as a rough means of visualizing the comparisons between the various age groups of patients with dementia paralytica and those of the population living at that age, as is done especially in chart 2.

CONCLUSIONS

Therefore, it is noted that, although the incidence of females in whom serologic tests for syphilis are positive may be equal to that of males in such a group as that present at Cook County Hospital, the female suffers less from dementia paralytica than the male. The female possesses some resistance which prevents neurosyphilis. I would suggest that the biochemical changes in the female associated with the menstrual cycle may be the factors which account for this immunity.

SUMMARY

1. It is pointed out that susceptibility to disease may be affected by racial, constitutional or sexual factors.

2. The biochemical changes incident to nonspecific protein therapy exert a marked effect on the course of syphilis, and are especially efficacious in the treatment of neurosyphilis.

3. The changes in the female occurring during the menstrual cycle are in some respects comparable to those occurring following nonspecific protein therapy.

4. The incidence of early syphilis in females apparently is equal to that in males in the same social group.

5. The incidence of dementia paralytica in females as compared to males is decidedly lower, 1 : 3.

6. The peak of the dementia paralytica rate in the female occurs approximately twenty years after that of the male; this lag is probably associated with the loss of protection which had been afforded by the menstrual cycle.

7. The biochemical changes incident to the menstrual cycle are probably responsible for this apparent immunity.

1817 West Polk Street.

LENARD OR CATHODE "RAY" DERMATITIS

STANLEY CRAWFORD, M.D.
PITTSBURGH

Dermatitis ranging from simple erythema to destruction of tissue resulting from irradiation with roentgen rays is well known since the introduction of these rays into medicine from the physicist's laboratory in 1896. The x-ray tube has proved of inestimable value in the diagnosis and treatment of pathologic conditions, and unmeasured thanks are due those physicists (Geissler, Plucker, Hittorf, Crookes, Hertz, Lenard, Roentgen, Jackson, Coolidge and others) who developed it.

Less known in medicine is the cathode tube which is used solely for the production of the cathode stream and still remains solely for experimental use in the laboratory of the physicist. The cathode stream, which is electronic and not electromagnetic and therefore is wrongly called "rays," was discovered by Sir William Crookes in 1878 while he was passing an electric current across a gap in a discharge tube having a vacuity of one-millionth of an atmosphere. In 1892, Heinrick Hertz discovered that the cathode stream would penetrate thin gold or aluminum foil contained within the tube, and his assistant and successor, Philip Lenard,[1] in 1894, after the death of Hertz, found that thin aluminum foil, 0.0026 mm. in thickness, cemented over an opening 1.7 mm. wide in a brass plate or cap at the discharge end of the tube would bear the atmospheric pressure and act as a window, allowing the cathode stream to pass through it from the tube into the air. The cathode stream passing through the thin aluminum directly into the atmosphere showed a luminosity for a distance of 5 cm. when operated by a voltage corresponding to a 3 cm. small sphere gap. Fluorescent materials became luminous in its rays up to a distance of 8 cm. from the window. This was the first successful cathode ray tube. If Lenard had placed his hand in the cathode stream in front of a photographic plate, as Roentgen accidentally did one year later, he would have discovered the x-rays.

In 1897 Thompson proved that the cathode "rays" consisted of particles (electrons) a thousand times smaller[2] than an atom of hydrogen. Jackson later discovered that the cathode stream could be focused by making its source cup-shaped.

The original Lenard tube, which had an aluminum cathode and was energized by an induction coil, has undergone several modifications. Pauli,[3] in 1910, redesigned the window at the discharge end with a brass

1. Lenard, P.: Ann. de physiol. **51**:225, 1894.
2. Actually 1,700 times smaller than an atom of hydrogen.
3. Pauli: Ztschr. f. Instrumentenk. **30**:133, 1910.

plate having twenty 2 mm. holes, 1 mm. apart, covered with thin aluminum foil supported by thin copper gauze. In 1920, Pauli [4] substituted a sheet of platinum with a 0.01 mm. hole for the aluminum foil. Krüger and Utesch [5] in 1925 designed a tube with a high vacuum, a hot cathode and a brass plate window with sixty-five 0.8 mm. holes which were water-cooled. A thin sheet of aluminum 0.005 mm. in thickness was cemented on the brass plate with picein. This tube was activated by a high tension transformer up to 60 kilovolts.

In the x-ray tube the cathode beam is confined in a short space between its source in a molybdenum focusing cup containing a flat spiral filament of tungsten wire heated to luminosity and a solid tungsten anode on which the cathode beam (electronic) impinges to create x-rays (electromagnetic pulsations).

In the cathode tube (commonly called the Lenard tube, just as the present-day x-ray tube is called the Coolidge tube) the molybdenum focusing cup containing a flat spiral of tungsten filament sends its beam a greater distance against a perforated or grid anode which allows over 80 per cent of the cathode stream to pass through uninterrupted. A window of thin aluminum or special nickel foil is mounted over the perforations, acting as anode and maintaining the vacuity of the tube through which the cathode stream readily passes with a negligible amount of interruption out of the tube into the air. Electrons, being more than a thousand times smaller than an atom, are therefore readily forced through the atomic structural planes of a thin material, such as gold, platinum, aluminum, nickel or special glass,[6] just as particles of dust can be blown through a fabric of silk, cotton or wool. The cathode stream is made up of negatively charged corpuscular electrons identical with the beta "rays" of radium except that they have one-third less

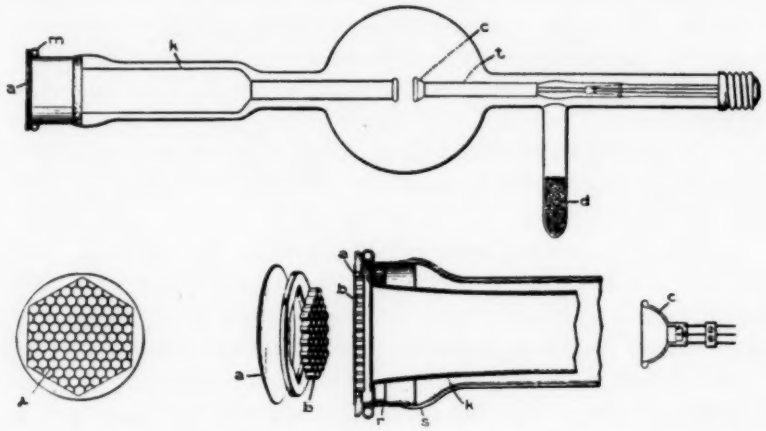
4. Pauli: Physiol. Ztschr. **21**:11, 1920.

5. Krüger and Utesch: Ann. de physiol. **78**:113, 1925.

6. A Lenard or cathode ray tube is now made which eliminates the metal foil window mounted on a metal grid by using a reentrant or inwardly concaved window of special glass so thin (0.005 inch [0.125 mm.]) that the electron beam of the cathode stream readily passes through it. This tube may be operated with an induction coil or with an x-ray generator giving constant direct current. It will not operate when connected directly to the x-ray transformer because the voltage thus supplied pulsates between zero and its maximum value sixty times per second, and the voltage, while increasing or decreasing during the first part or the last part of one of these pulsations produces a stream of electrons of less penetrating power, which are absorbed by a thin glass window causing local heating and consequent puncturing of the glass. This is avoided by the maintenance of a constant stream of electrons of high penetrating power by the use of direct current. When the tube is operated at 120 kilovolts, the electrons emerge from the window with an approximate velocity of 125,000 miles per second with a range of about 8 inches in the atmosphere. (This tube is made by the Westinghouse Lamp Company, Bloomfield, New Jersey, and was designed by Dr. C. M. Slack.)

velocity, 40,000 miles per second, and are correspondingly less penetrating. The velocity of the cathode stream of electrons depends directly on the voltage used in generating them in a vacuum discharge tube. When they are passed through a thin metal or glass window into the surrounding air they are known as Lenard rays. Therefore, the speed of the Lenard rays depends on the voltage used in the creation of the cathode stream and on the penetrability of the window. The cathode rays produce x-rays when impinged on an object just as the beta rays of radium produce gamma rays when they are intercepted.

The modern high voltage cathode tube, like the modern high voltage x-ray tube, has been a development attributable to W. D. Coolidge. In 1926, Coolidge [7] developed the modern Lenard or cathode tube. It has an overall length ranging from 50 to 150 cm. and a cathode of tungsten



The Coolidge high voltage cathode tube: (*a*) Anode and window of sheet nickel foil 0.0127 mm. thick and 7.5 cm. in diameter; (*b*) anode-window support of honeycomb structure of sheet molybdenum 0.015 cm. thick bent into hexagonal cells fastened together and to the surrounding molybdenum frame by copper brazing in hydrogen, each cell being 0.6 cm. wide and 0.47 cm. deep; (*r*) Invar ring to which the edge of the nickel foil window is soldered and which is sealed directly to the end of the glass anode arm at *S;* (*k*) long copper tube electrostatic shield, electrically connected to the window, to protect the glass of the anode arm from puncturing; (*c*) cathode of hemispherical molybdenum cup 2.5 cm. in diameter containing tungsten filament 0.0216 cm. in diameter coiled into a flat spiral 0.5 cm. in diameter; (*t*) molybdenum tube covering the cathode support wires; (*m*) single twin copper coil for water-cooling the window support; (*d*) side tube containing cocoanut charcoal to connect with exhaust pump if used. (The diagram and description are published with the permission of Dr. W. D. Coolidge and the *Journal of the Franklin Institute.*)

7. Coolidge, W. D.: The Production of High-Voltage Cathode Rays Outside of Generating Tube, J. Franklin Inst. **202**:693 (Dec.) 1926.

wire 0.0216 mm. thick arranged in a flat spiral 0.5 cm. wide which occupies the recess of a hemispherical molybdenum focusing cup 2.5 cm. in diameter. The entire cathode beam is directed to a brass window along a shield of copper tubing in such a way that very little of the rays impinge on the side of the tubing. This copper shield acts as an electrostatic barrier, preventing an accumulation of the cathode potential from rupturing the glass arm of the tube during high voltage operation and also preventing the production of x-rays and the heating of the anode arm. Most of the electrons of the cathode stream pass through the window, and very few strike the glass because of the tubular copper shield. Electrons reflected from the window and its support strike the shield, and very few can pass back through the shield or emerge from its inner end against the direction of the cathode stream.

The window is of specially made nickel foil 0.0127 mm. thick or of a special alloy known as no. 4 Resistal which is made of chromium, silicon, carbon, iron and nickel which is supported by a honeycomb structure of sheet molybdenum, the hexagonal cells of which are 0.6 cm. wide and 0.47 cm. deep. These cells are fastened together by copper brazing and then fastened into a molybdenum ring. The tube is operated with a high tension transformer at from 60 to 200 kilovolts and even at higher voltages.

Cathode rays have a marked biologic effect on plant and animal tissues. They kill bacterial organisms, stunt the growth of seeds and alter the growth of animal tissue. In a larger dosage they cause destruction of tissue. Knudson found that the antirachitic value (vitamin D) of yeast is increased by irradiation with cathode rays just as much as by irradiation with ultraviolet rays. Cathode rays have also been used in photographing thin substances and will cause fluorescence of certain minerals, such as calcite or rock salt. An interesting series of experiments with these rays was published by Coolidge [8] in 1926.

Because of the rarity of reports of cathode or Lenard ray "burns" in medical literature it is of interest to record a case.

REPORT OF A CASE

X. Y. Z., aged 26, a research physicist in an industrial laboratory, inadvertently exposed the dorsal surface of his right hand and fingers to cathode rays from a Lenard tube while making diffraction experiments. This exposure was made on four successive days, at times under a willemite screen, with an approximate total exposure of ten minutes. The tube was operated with 3 milliamperes of current at 75 kilovolts, a spherical spark gap of 50 mm., or approximately 2 inches, and a needle point spark gap of 160 mm., or 6½ inches. The maximum estimated wave-

8. Coolidge, W. D., and Moore, C. N.: Some Experiments with High Voltage Cathode Rays Outside of Generating Tube, J. Franklin Inst. **202**:721 (Dec.) 1926.

length associated with the cathode beam was approximately 0.06 angstroms, the equivalent of very hard x-rays. The distance of the hand from the window of the tube averaged from 12 to 20 cm. Three days later he noticed a slight redness over the back of the hand and fingers, more marked on the index and middle fingers. Ten days later the irradiated areas showed marked redness with slight edema. The dorsal surface of the first phalangeal areas of the index finger, the first, second and third phalangeal areas of the middle finger and the mesial half of the distal phalangeal area of the ring finger presented flat bullae fourteen days later. The redness was abruptly marginated in a straight line diagonally across the dorsal surface of the right hand from the base of the ring finger to the proximal end of the first metacarpal. With the application of soothing dressings the reaction healed in about four weeks. Ten months later the distal and middle phalangeal areas of the index, middle and ring fingers showed numerous areas of telangiectasia on their dorsal surfaces with dryness and a scarcely perceptible thinning of the cutis. The nails did not show any abnormal alteration. The hair follicles and hairs were absent from the middle phalangeal areas of the fingers involved. The rest of the hand appeared to be normal.

1202 Westinghouse Building.

SULPHUR CONTENT OF HAIR AND OF NAILS IN ABNORMAL STATES

THERAPEUTIC VALUE OF HYDROLYZED WOOL; I. HAIR

HERMAN BROWN, B.S.
AND
JOSEPH V. KLAUDER, M.D.
PHILADELPHIA

Keratin, a simple protein of albuminoid nature, is the chief constituent of hair, indeed of all epidermal tissue—nails, feathers, horns and hoofs. Keratin is peculiar, in that it has a high sulphur content, the sulphur being present almost entirely in the form of the amino-acid cystine. No other protein is so high in cystine as the keratin of human hair. It would appear, therefore, that the metabolism of sulphur probably plays an important rôle in the development and growth of these tissues.

SULPHUR AND CYSTINE CONTENT OF KERATIN; RELATION OF CYSTINE TO GROWTH OF HAIR

Vauquelin,[1] in 1806, was apparently the first to report the chemical composition of hair. He found that hair contained considerable sulphur, and that white, blond and red hair contained more sulphur than black hair. Later, van Laer [1] found that the sulphur content of hair of men varied between 4.6 and 5.4 per cent. The average sulphur content of fifteen samples of human hair was found by von Bibra [1] to be 4.62 per cent. The variation ranged from 3.83 to 8.23 per cent. The latter figure was that for red hair. Mohr [2] found 4.95 per cent of sulphur in the hair of a woman, whereas the hair of a girl, aged 9, contained 5.34 per cent; the hair of a boy, aged 4, contained 4.98 per cent, and the red hair of a boy, aged 6, contained 5.32 per cent.

In hair from Indians, Japanese, Negroes and Caucasians, Rutherford and Hawk [3] found that the sulphur varied from 4.82 to 5.22 per cent.

From the Research Institute of Cutaneous Medicine.

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 4, 1932.

1. Quoted by Rutherford and Hawk.[3]

2. Mohr, P.: Ueber den Schwefelgehalt verschiedener Keratinsubstanzen, Ztschr. f. physiol. Chem. **20**:403, 1895.

3. Rutherford, T. A., and Hawk, P. B.: A Study of the Comparative Chemical Composition of the Hair of Different Races, J. Biol. Chem. **3**:459, 1907.

The sulphur content of nails was found by Mulder [4] to be 2.80 per cent. Horbaczewski [5] found 3.2 per cent of sulphur in horn.

The figures for the sulphur and cystine contents of the more common types of keratin have varied as reported by various observers, depending on the degree of purification of the keratins, the methods of preliminary treatment and the determination of cystine. An entirely satisfactory method for the determination of cystine is lacking. Wilson and Lewis [6] determined the cystine and sulphur contents of a considerable number of keratins by a uniform procedure. Their results afford a more extensive comparative study of the keratins than has been available [7] heretofore.

The comprehensive study of Wilson and Lewis [6] is pertinent and will be reviewed briefly. The cystine content of hair and wool of various species and of tortoise shell, feathers and skin was studied. Human hair gave values from 15.6 to 21.2 per cent; sheep wool, from 8 to 10.9 per cent; feathers, from 7.05 to 12.2 per cent; rabbit hair, from 11.9 to 14 per cent; tortoise shell, from 6.4 to 8.1 per cent; rat hair, 14.1 per cent; cat hair, 13.1 per cent, and dog hair, 19 per cent.

Although the sulphur and nitrogen values of keratins from individuals of a species varied rather widely, the ratio of nitrogen to sulphur was relatively constant for that particular keratin.

Three samples of human skin and one of human connective tissue were analyzed. The cystine content was lower (from 1.82 to 2.34 per cent) and the nitrogen to sulphur ratio (23 to 25 per cent) was higher than those for human hair.

Relationship was not evident between the cystine content of human hair and the color of the hair, the age or the sex of the individual. Little evidence was obtainable of the existence of significant amounts of noncystine sulphur in the keratins studied.

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4. Mulder, G. J.: Versuch einer allgemeinen physiologischen Chemie, Braunschweig, F. Vieweg u. Sohn, 1844-1851.

5. Horbaczewski, in Ladenburg, A.: Handwörterbuch der Chemie, Breslau, Eduard Trewendt, 1885, vol. 3.

6. Wilson, R. H., and Lewis, H. B.: The Cystine Content of Hair and Other Epidermal Tissues, J. Biol. Chem. **73**:543, 1927.

7. Wilson and Lewis determined cystine colorimetrically by the method of Folin and Looney. In their paper other methods for the determination of cystine are discussed. See also: (*a*) Sullivan, M. X.: Studies in the Biochemistry of Sulphur: A Distinctive Test for Cystine, Pub. Health Rep. **41**:1030, 1926; **44**:1421, 1929. (*b*) Smuts, D. B.; Mitchell, H. H., and Hamilton, T. S.: The Relation Between Dietary Cystine and the Growth and Cystine Content of Hair in the Rat, J. Biol. Chem. **95**:285, 1932.

Rimington,[8] Sullivan and Hess [9] and Barritt and Rimington [10] have shown that practically the entire sulphur content of purified wool and animal hair can be accounted for as cystine, a notable exception being that of camel hair.

It appears, therefore, that sulphur in hair is almost entirely in protein combination as the amino-acid cystine.

Freund [11] isolated twelve different amino-acids from horse as well as from camel hair.

A number of investigators, in pursuing studies in nutrition on laboratory animals, have noted incidentally a relationship of the protein content of the diet to the growth of hair. In a study conducted by Abderhalden,[12] a full growth of hair was produced on a dog during the time the animal was fed a diet containing completely hydrolyzed protein as the sole source of nitrogen. McCollum, Simmonds and Parsons [13] observed loss of hair in white rats fed on diets containing a low percentage of protein, mostly from potato. Boas [14] made a similar observation following a diet in which a commercial preparation of egg white was the sole source of protein. Improvement was obtained by the substitution of either 20 per cent casein or serum albumin for the protein of the egg white.

Evvard, Dox and Guernsey [15] suggested, from observations on the character of the growth of hair on litters of sows fed "black albumin" during pregnancy, that the production of hair is related to a diet containing the amino-acid cystine.

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8. Rimington, C.: The Relation Between Cystine Yield and Total Sulphur in Wool, Biochem. J. **23**:41, 1929; The Relation Between Cystine Yield and Total Sulphur in Various Animal Hairs, ibid. **23**:726, 1929.

9. Sullivan, M. X., and Hess, W. C.: Studies on the Biochemistry of Sulphur: VII. The Cystine Content of Purified Proteins, Pub. Health Rep., 1930, supp. 86, p. 1.

10. Barritt, J., and Rimington, C.: The Relation Between Total Sulphur and Cystine Content of Certain Samples of Rabbit Fur, Biochem. J. **25**:1072, 1931.

11. Freund, E.: Chemie der Haut, in Truttwin: Kosmetische Chemie, quoted by Perutz, A.: Pharmakologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, pt. 1, p. 228.

12. Abderhalden, E.: Weitere Versuche über die synthetischen Fähigkeiten des Organismus des Hundes, Ztschr. f. physiol. Chem. **83**:444, 1913.

13. McCollum, E. V.; Simmonds, N., and Parsons, H. T.: The Dietary Properties of the Potato, J. Biol. Chem. **36**:197, 1918.

14. Boas, M.: Further Note on the Value of Egg White as the Sole Source of Nitrogen for Young Growing Rats, Biochem. J. **18**:1322, 1924.

15. Evvard, J. M.; Dox, A. W., and Guernsey, S. C.: The Effect of Calcium and Protein Fed Pregnant Swine upon the Size, Vigor, Bone, Coat and Condition of the Offspring, Am. J. Physiol. **33-34**:312, 1914.

Hartwell [16] observed that young rats frequently suffered loss of fur when fed on a diet poor in protein or in which a poor quality protein was the only source of amino-acids. This condition could be remedied by improving the ration of protein, either in quality or in quantity. In her experiments, a loss of fur was obtained when potato or white bread was the sole source of protein. The addition of gluten, gelatin or caseinogen to the bread diet prevented completely the loss of fur. Brown bread or oatmeal as the sole source of protein resulted in no loss of fur.

Abelin [17] produced loss of hair in white rats after feeding an exclusive diet of zwieback. Hair was restored by the addition of thyroid gland to the diet and also by the addition of from 0.050 to 0.075 Gm. of cystine daily.

Lightbody and Lewis [18] comprehensively studied the relation of cystine to the production of hair in white rats. The animals were fed diets varying only in their protein content, i. e., diets in which the amount of cystine had been shown to be the limiting factor. The purpose was to determine whether in cases of an inadequate supply of cystine in the diet, the demand for cystine for the growth of more essential tissue and for the elaboration of the less essential epidermal structure, the hair, cannot be met. Will the demand for cystine for purposes of growth take precedence over the requirements for the production of hair?

It was shown that the amount of hair produced, like the somatic development, was related to the protein (and cystine) content of the diet, but under the experimental conditions of the study, the demands for protein (and cystine) for the growth of the hair appeared to be secondary in importance to the demands for the growth of the body with its more essential tissues.

In another study,[19] Lightbody and Lewis conducted experiments in the direction of showing whether the amounts of cystine and sulphur present in hair were influenced by factors of age or diet. They found that the cystine and sulphur contents of the hair of the white rat varied with the cystine content of the diet and, to some extent, with the age

16. Hartwell, G. A.: A Possible Correlation Between Dietary Protein and Loss of Fur in Young Growing Rats, Biochem. J. **19**:75, 1925.

17. Abelin, I.: Experimentelle Erzeugung von Haarausfall und Haarwachstum, Dermat. Wchnschr. **91**:1475, 1930.

18. Lightbody, H. D., and Lewis, H. B.: The Metabolism of Sulfur: Relation of the Protein and Cystine Content of the Diet to the Growth of Hair in the White Rat, J. Biol. Chem. **82**:485, 1929.

19. Lightbody, H. D., and Lewis, H. B.: The Metabolism of Sulfur: Dietary Factors in Relation to the Chemical Composition of the Hair of the Young White Rat, J. Biol. Chem. **82**:663, 1929.

of the animals. The cystine and sulphur contents of the hair of young rats ("puppy" coat) were significantly lower than those of the hair of rats fed on diets high in their content of cystine. Hair from animals on a diet in which cystine was the factor limiting growth resembled in its lower cystine and sulphur contents the first coat of air produced in young rats. Retardation of growth alone did not produce a hair low in cystine content, since a diet deficient in some factor other than cystine, e. g., lysine, did not result in the production of a hair of abnormally low cystine or sulphur content.

Beadles, Braman and Mitchell [20] concluded from their experiments that the addition of cystine to a diet the protein content of which was so low as to be the limiting factor in growth and which was deficient in this amino-acid increased its value in the promotion of hair growth in the albino rat. The coat of hair produced on such rations, when supplemented with cystine, was not only heavier in toto, but heavier per unit of surface area. It appeared, therefore, that under these conditions the growth of hair had been stimulated to a greater extent by the cystine supplement than had the growth of all tissues as measured by an increase in body surface. There was no indication that the demands of the more vital tissues for cystine had taken precedence over the demands of the hair follicles.

More recently, Smuts, Mitchell and Hamilton [7b] studied the influence of cystine on hair. They concluded that a ration deficient in cystine inhibits body growth and, too, the growth of hair, measured in dry weight per unit of surface. Furthermore, the smaller growth of hair contains a smaller content of cystine than hair produced on the same ration to which a small amount of cystine has been added. This cystine-deficient coat of hair, although consisting in the main of hair fibers possessing a normal histologic structure, contains a certain proportion of hair fibers the medullary cells of which are broader in shape and loosely packed together. In such hairs, the proportion of cortex, representing the completely keratinized part of the hair according to the studies of Barritt and King,[21] is much less than in the normal hair, while the proportion of hair cells and medullary cells consisting of sulphur-poor substance is correspondingly greater.

Barritt and King [21] have made interesting microscopic studies in an endeavor to explain the wide variability in the sulphur content of wool.

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20. Beadles, J. R.; Braman, W. W., and Mitchell, H. H.: The Relation Between Cystine Deficiency in the Diet and Growth of Hair in the White Rat, J. Biol. Chem. **88**:623, 1930.

21. Barritt, J., and King, A. T.: Note on the Sulphur-Free Nature of Medulla in Blackface Wool, Biochem. J. **25**:1075, 1931.

They observed that variations in the sulphur content were associated with variations in the proportion of medullated fibers or in the proportion of medulla in a single fiber.

Smuts, Mitchell and Hamilton further concluded that an addition of cystine to a cystine-deficient diet corrects its effects on body growth, hair growth and hair composition; an addition of cystine to a diet with no such deficiency has no certain effect on the composition of hair. A ration deficient in lysine inhibits body growth and also the growth of hair, but the cystine content of the hair produced is not lowered.

THERAPEUTIC USE OF KERATIN TO PROMOTE THE GROWTH OF HUMAN HAIR; REVIEW OF THE LITERATURE

Zuntz [22] prepared and employed clinically hydrolysates of horn to promote the growth of hair in man [23] and of wool in sheep. In his communication the method of making this preparation is lacking.[24] It is administered internally in pill form, in a total daily dose of about 1.5 Gm. Zuntz reported good results in promoting the growth of hair on himself and in others, and likewise in increasing the growth of wool in experiments on sheep.[25]

Conflicting reports have appeared relative to the value of this preparation to promote the growth of human hair.

Matoni [26] reported good results with the keratin preparation in patients with alopecia which followed infectious disease, but no results in patients with alopecia seborrheica or in young patients with diffuse loss of hair. In women, an undesirable growth of hair may appear on the face and chest following its use.

Blaschko [27] administered the keratin preparation to sixty patients with alopecia areata, in whom light therapy had been employed unsuccessfully. In another group, light therapy was employed conjointly

22. Zuntz, N.: Beeinflussung des Wachstums der Horngebilde (Haare, Nägel, Epidermis) durch spezifische Ernährung, Deutsche med. Wchnschr. **46**:145, 1920.

23. According to A. Perutz (Pharmakologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, pt. 1, p. 228), keratin was first used by Kreibach to promote the growth of human hair.

24. Burow (quoted by Polland [34]) gave the following chemical analysis of the keratin preparation: Anions: chlorine, phosphoric acid and sulphuric acid. Kations: iron, calcium, magnesium, sodium and potassium; cystine and tyrosin. Tryptophan was absent.

25. Zuntz, N.: Zur Hebung des Wollertrages unserer Schafe, Jahresb. u. d. Fortschr. d. Thierchem. **49**:594, 1919.

26. Matoni, H. H.: Die Bedeutung der spezifischen Ernährung der Horngebilde durch Humagsolan seine Anwendung und Erfolge, Med. Klin. **20**:1432, 1924.

27. Blaschko, A.: Die Behandlung von Haarerkrankungen mit löslichen Hornpräparaten, Deutsche med. Wchnschr. **46**:512, 1920.

with the preparation. The best results were obtained in this group. From this study, Blaschko concluded: In a few patients the results were indisputable; there was a complete restoration of hair. In others, especially with advanced cases, the therapy was a complete failure. In the majority of patients a considerable improvement was obtained.

Saalfeld [28] obtained good results in "many cases" with loss of hair. He stated that the preparation has a general tonic action. He advised the concomitant use of external measures.

Fuhs [29] employed the keratin preparation unsuccessfully in the treatment of alopecia areata and alopecia seborrheica. He observed no increase in the growth of hair of normal persons and no increase in the growth of nails.

Klinke [30] observed a good result in the treatment of one patient with ringed hair. Following the use of the preparation he noted a slight increase in the sulphur and cystine contents of the hair.

Kapp [31] employed locally keratin digested in ammonium hydroxide and then incorporated in from 10 to 20 per cent ointment. This was applied daily for from three to five months. In 90 per cent of the patients treated, good results were obtained. He also applied this keratin solution by galvanic current. In another group he employed the patient's own hair or nails by digesting them in ammonium hydroxide. He reported good results from such treatment.

Jessner [32] stated that the preparation is ineffective in man. He from his experiments with guinea-pigs and Loewe and Faure [33] from their experiments with rabbits concluded that the keratin preparation was ineffective in promoting the growth of hair in these animals.

Polland [34] observed good results from the prolonged administration of the keratin preparation. However, in his opinion, these results could not with certainty be attributed to this preparation.

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28. Saalfeld, E.: Zur Behandlung des Haarausfalles, Med. Klin. **23**:907, 1927.

29. Fuhs, H.: Ueber die Wirksamkeit des Zuntzschen Haarwuchsmittels Humagsolan, Wien. klin. Wchnschr. **33**:707, 1920.

30. Klinke, K.: Pigmentstudien im Anschluss an einen Fall von Ringelhaar, Biochem. Ztschr. **160**:28, 1925.

31. Kapp, J. F.: Ueber lokale Therapie der Alopecia seborrhoica mit "Keratin," insbesondere auf contophoretischem Wege, Deutsche med. Wchnschr. **47**:296, 1921.

32. Jessner, M.: Zur experimentellen Prüfung von Haarwuchsmitteln und über das Wiederwachsen der Haare an rasierter Rattenhaut, Klin. Wchnschr. **3**:2195, 1924.

33. Loewe, S., and Faure, W.: Zur experimentellen Prüfung von Haarwuchsmitteln (Humagsolan), Klin. Wchnschr. **3**:1532, 1924.

34. R. Polland reported good results in promoting the growth of hair, as observed clinically, from the local use of a colloidal solution containing the amino-acids present in keratin (Erfahrungen mit neuen Haarwuchsmitteln, Dermat. Wchnschr. **93**:1953, 1931).

Levin and Ohman [35] conducted experiments in man and also in rabbits. In man, an increase of from 10 to 20 per cent in the growth of hair was noted after the administration of the keratin preparation. In rabbits, the growth of hair was also increased. From these experiments, the authors are convinced that the preparation has hair-building powers.

Kitahara [36] administered to patients with alopecia a brown powder prepared from human hair by Aschi. It was given by mouth in doses of from 0.05 to 0.15 Gm. per day. The report embraces a series of one hundred and five cases. In less severe cases of alopecia areata, complete regrowth of hair occurred after the administration of the preparation for seven weeks; in the more severe cases, after several months. In alopecia seborrheica, complete regrowth of hair in men occurred after from two to six weeks; in women, after a longer time.

Nakagawa and Shimomura [37] employed a synthetic mixture in the treatment of alopecia areata. The preparation consisted of two solutions: The first contained cystine and tyrosine, alkali metals, phosphorus and arsenic; the second contained potassium, calcium, phosphorus and iron. Two cubic centimeters of the first solution was mixed with 0.5 cc. of the second and injected subcutaneously daily or every other day. Twenty-five patients with alopecia areata, varying from a single spot to alopecia totalis, were given injections for periods of from one to six months, depending on the results. Of the number treated, nineteen were completely cured, four were almost cured, and two showed no improvement.

Forster [38] studied the value of externally applied agents in promoting the growth of hair in laboratory animals. Of the various preparations studied, one was a 2 per cent cystine in ointment; another, hydrosolate of human hair. He failed to demonstrate any value in these or in other agents studied which were alleged to promote the growth of hair. Mechanical irritation appeared to be the chief factor in promoting the growth of hair.

Abderhalden and Wertheimer [39] failed to influence the growth of hair in guinea-pigs by subcutaneous injections of extracts of hair, feathers and skin.

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35. Levin, E., and Ohman, H.: The Influence of Keratin on Hair Growth, Svenska läk.-tidning. **22**:769, 1925.

36. Kitahara, Y.: Experimentelle und klinische Studien über die Wirkung eines neuen Haarwuchsmittels "Genka," Jap. J. Dermat. & Urol. **24**:539, 1924.

37. Nakagawa, K., and Shimomura, A.: A Novel Method for Treating Alopecia, Jap. J. Dermat. & Urol. **25**:38, 1925.

38. Forster, A.: Beeinflussung des Haarwachstums durch äusserliche Mittel, Arch. f. exper. Path. u. Pharmakol. **144**:363, 1929.

39. Abderhalden and Wertheimer: Weitere Beiträge zur Kenntnis von organischen Nährungsstoffen mit spezifischer Wirkung, Arch. f. d. ges. Physiol. **191**:258, 1921.

THE PREPARATION OF CYSTINE FROM KERATIN-HYDROLYZED WOOL

In view of the foregoing data, it was thought desirable to reinvestigate the therapeutic use of keratin in the treatment of loss of hair in man. It did not seem desirable to administer cystine per se as a therapeutic agent, since the cost of this preparation makes its employment impracticable; moreover, it appears more pertinent to utilize all the constituents of keratin. Ground fish scales were considered for internal administration. The strong odor and the uncertainty of digestion, however, excluded their use. Of other available keratins, wool was selected from which to prepare cystine, since it is inexpensive and easily obtainable in a clean state, washed and scoured, free from grease and extraneous material. Its cystine content, although less than that of "human hair," is relatively high, from 8 to 11 per cent. Wool can be readily hydrolyzed, making of the insoluble, indigestible keratin an easily soluble mixture of amino-acids which can be readily absorbed. Such a preparation, which can be easily administered, will contain not only cystine but other amino-acids; indeed, all the primary constituents of wool that may be concerned in the growth of epidermal tissue containing keratin. In the foregoing regard, the thought of hormones being present in hair or wool, influencing the growth of such tissues, is appropriate and not unreasonable, although the method of digesting wool may destroy such hormones.

Accordingly, wool was hydrolyzed in the following way: To 4 pounds (1.8 Kg.) of white wool in a 5 liter round bottom flask add 1,000 cc. of concentrated hydrochloric acid and 1,000 cc. of water. Connect to the reflux air condenser and boil slowly for four hours. Cool. Add, with constant cooling, 40 per cent sodium hydroxide until faintly acid. Filter. Hydrolyzed wool thus prepared is a dark brown liquid having an odor of sulphur. The cystine content is about 1.5 Gm. per 32 cc. After prolonged standing, a dark brown precipitate forms which is dissolved by the addition of water.

Relative to the absorption of hydrolyzed wool after ingestion, such absorption, at least of cystine, apparently occurred in the experiments on rabbits, to be presented later. Sullivan and Hess [40] and others have shown that cystine is absorbed from the gastro-intestinal tract of white rats.

To our knowledge, hydrolyzed wool has not been employed as a therapeutic agent to promote the growth of hair. This statement may possibly apply to any of the other keratins administered in a soluble state, and hence containing all the amino-acids present in such keratin.

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40. Sullivan, M. X., and Hess, W. C.: Studies on the Biochemistry of Sulphur, Pub. Health Rep. **46**:390, 1931.

HYDROLYZED WOOL IN PROMOTING GROWTH OF HAIR

Laboratory Study.—Eight rabbits were placed on a cystine-poor diet consisting of casein, 15 Gm.; oat straw, 12 Gm.; dextrin, 45 Gm.; lactose, 25 Gm., and salt mixture, 3 Gm., containing dibasic potassium phosphate, 1 cc.; sodium chloride, 1 cc.; magnesium sulphate, 0.5 cc., and citric acid, 0.5 cc.

Four rabbits died before the expiration of five weeks. After five weeks of feeding on the purified diet, the four remaining rabbits were treated in the following way: The hair on one half of one side of each animal was removed by barium sulphide. To the cystine-poor diet of two of the animals (rabbits 4 T and 3 T) was added 3 cc. of hydrolyzed wool, administered three times daily. The cystine-poor diet alone was continued in the two remaining animals (rabbits 3 and 6 T). The two rabbits receiving the hydrolyzed wool regrew hair in contrast to the animals to which hydrolyzed wool was not administered. Control rabbits, housed under the same conditions and fed normal diets, regrew hair in one month sufficient to cover bald areas of the same size as the areas on the experimental animals.

The results are graphically represented in figures 1, 2 and 3. The animal in figure 1 *A* (rabbit 6 T) was fed on the cystine-poor diet for five weeks; there was no regrowth of hair. Before the use of the cystine-poor diet, the sulphur content of hair was 3.80 per cent. Figure 1 *B* shows the same animal after ten weeks on the cystine-poor diet; the hair is still absent. The sulphur content of the hair at this time was 3.29 per cent. Figure 2 (rabbit T 4) shows regrowth of hair, three weeks after the addition of hydrolyzed wool to the cystine-poor diet. The sulphur content of the hair before the cystine-poor diet was 3.88 per cent. After five weeks of this diet, the sulphur content decreased to 3.62 per cent, and increased to 4.03 per cent after three weeks of hydrolyzed wool plus a cystine-poor diet. Figure 3 (rabbit 3 T) shows another animal with a greater regrowth of hair after five weeks of hydrolyzed wool supplementing a cystine-poor diet. Before the use of the cystine-poor diet, the sulphur content of the hair was 4.07 per cent; after five weeks of this diet, it was 3.78 per cent; after five weeks of hydrolyzed wool supplementing the cystine-poor diet, the sulphur content was 4.11 per cent. In another animal, the sulphur content of the hair was 4.02 per cent before the cystine-poor diet was used; after five weeks of such a diet, it was 3.93 per cent, and after ten weeks, 3.81 per cent. There was no regrowth of hair.

It should be noted that the increase or decrease of the sulphur content of hair, excepting the decrease in animal 6 T, was slight and within the error inherent in chemical analysis, which we regard as 0.2 per cent. It is significant, however, that the change in sulphur content was in the expected direction.

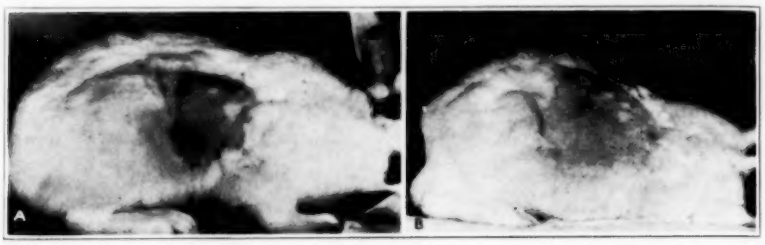

Fig. 1 (rabbit 6 T).—*A*, absence of regrowth of hair in rabbit fed on a cystine-poor diet for five weeks. Control rabbits on a normal diet regrew hair, which completely covered a similar bald area in four weeks. *B*, absence of hair after ten weeks on a cystine-poor diet. The sulphur content of the hair decreased from 3.80 to 3.29 per cent. Compare with figures 2 and 3.

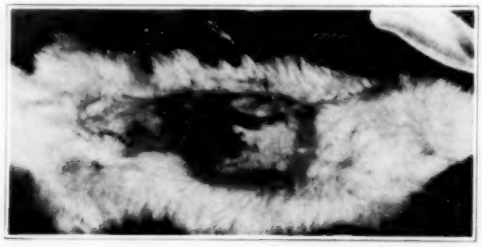

Fig. 2 (rabbit 4 T).—Regrowth of hair three weeks after supplementing a cystine-poor diet with hydrolyzed wool. The animal was fed a cystine-poor diet for six weeks, during which time no hair regrew. The sulphur content of the hair decreased from 3.88 to 3.62 per cent. After supplementing hydrolyzed wool with a cystine-poor diet, the sulphur content increased to 4.03 per cent.

Fig. 3 (rabbit 3 T).—Considerable regrowth of hair after five weeks of hydrolyzed wool supplementing a cystine-poor diet. The suulphur content of the hair decreased from 4.07 to 3.78 per cent after the cystine-poor diet and then increased to 4.11 per cent after hydrolyzed wool was added to the cystine-poor diet.

Hair in the rabbit regrows in islands or tufts, and hence these animals are not particularly adapted for experimental study of the growth of hair. However, the gross results of these experiments as shown in figures 1, 2 and 3, which correlated the study of the sulphur content of the hair of the same animals, were sufficiently decisive so that further experiments were deemed unnecessary.

From these studies it is concluded that hydrolyzed wool furnishes the requirements for the growth of hair in rabbits fed on a cystine-poor diet.

Clinical Study.—Forty patients of both sexes and different ages, with loss of hair attributed to various causes—alopecia areata (localized, diffuse, totalis) accompanying seborrhea following pregnancy, infectious disease and alopecia prematura—were given hydrolyzed wool. The preparation was administered by mouth, 2 teaspoonfuls in water, three times daily, to adults; one half of this amount was given to children. The administration of hydrolyzed wool was continued in the absence of other treatment; in some patients, for at least one month; in others, for from two to three months and longer.

In this study, only two outstanding favorable results were obtained. Both patients had alopecia areata totalis. One, a boy, aged 16, had universal loss of hair for three years. Different treatments were employed without success. About one month after the administration of hydrolyzed wool, there was evidence of growth of hair. Three months later the eyebrows were completely restored; hair was present, but not in normal amounts, in the axilla and pubic region; hair almost covered the scalp; there were, however, some patches of alopecia areata. The patient gained 8 pounds (3.6 Kg.). After taking hydrolyzed wool for seven months, regrowth of hair on the scalp was about normal except for a few patches of alopecia areata.

The second case was that of a man, aged 42, who had complete loss of hair for two years. After taking hydrolyzed wool for three weeks, there was evidence of regrowth of hair. After the administration of hydrolyzed wool for ten months, a normal amount of hair was present on the chest, axilla, pubic region, margins of the eyelids and eyebrows. The scalp was completely covered with hair, but the amount was not normal; there were scattered areas of alopecia areata and areas in which the hair was apigmented.

In two other patients with alopecia totalis, hydrolyzed wool administered for three months was ineffective. In one patient with alopecia areata, new bald areas appeared during the administration of hydrolyzed wool. The preparation was ineffective in young men with alopecia prematura and in patients with thin and scanty hair associated with seborrheic eczema. In many patients with alopecia areata, the prepara-

tion was ineffective. In others and also in some patients with loss of hair attributable to other causes, the hair regrew after the taking of hydrolyzed wool. It cannot be concluded, however, that this regrowth was attributed to the ingestion of hydrolyzed wool, since, in such patients, hair regrows in the absence of any treatment.[41]

SULPHUR CONTENT OF HAIR AND NAILS IN ABNORMAL STATES; INFLUENCE OF HYDROLYZED WOOL

To our knowledge, the sulphur content of hair in conditions associated with loss of hair has never been studied, nor has the sulphur content of nails in diseases or abnormalities of the nails. Such study is herewith reported and, in addition, the effect of hydrolyzed wool therapy on the sulphur content of hair or nails. Study of the nails is being separately reported. Sulphur was determined according to the method of Stockholm and Koch[42] and expressed as percentage of sulphur. The margin of error inherent in chemical analysis, we believe, is within 0.2 per cent.

We regard the normal percentage of sulphur in hair to range from 4.5 to 5.2. In six normal control patients the range was from 4.6 to 5.1 per cent, an average of 4.86. This compared with a normal average of 4.62 per cent, as given by von Bibra,[1] and a range of from 4.82 to 5.2 per cent, as given by Rutherford and Hawk.[3]

Hydrolyzed wool was administered to all patients with alopecia areata. In six, a single analysis of hair was made before such administration; this group showed an average percentage of sulphur of 4.38. In six other patients, a single analysis of hair was made after variable periods of administration of hydrolyzed wool. It is significant that the average percentage of sulphur in this group was 5.5. This difference, favorable to hydrolyzed wool therapy, was not as favorably expressed in clinical improvement, since, as previously stated, outstanding results were obtained in only two patients, each of whom had alopecia totalis.

41. In clinical experimentation involving the efficacy of a therapeutic agent, conclusion is invariably *post hoc*, since adequate control experiments are not possible. Our experience with the following case is pertinent. A patient previously seen with alopecia totalis was again asked to come in order that hydrolyzed wool be prescribed. At the time of her return to the clinic, hair had started to regrow two months previously in the absence of any treatment. However, hydrolyzed wool was administered. The hair continued to grow, but such regrowth was not more rapid than before the use of hydrolyzed wool. Four months after the onset of regrowth of hair and after two months' use of hydrolyzed wool, a specimen of hair contained 5.3 per cent of sulphur.

42. Stockholm, M., and Koch, F. C.: A Quantitative Method for the Determination of Total Sulfur in Biological Material, J. Chem. Soc. **45**:1953, 1923.

The three highest individual percentages of sulphur, 5.3, 5.3 and 5.6, in the entire series were obtained in this group. These patients were taking hydrolyzed wool for months before analysis of the hair was made, and at the time hair was regrowing.

A group of nine subjects, including patients with alopecia (young men), those with alopecia senilis and three young women with loss of hair, showed an average percentage of sulphur of 4.28. This percentage we regard as subnormal. The two lowest percentages of sulphur for any patient in the entire series were obtained in this group—3.9 (case 46) and 3.8 (case 48). In one of these patients, a young woman (case 46) who had a definite loss of hair, it is significant that her diet was low in animal protein; milk and cheese in any form had not been eaten for years; eggs, meat and fish were eaten only occasionally. This possible dietary factor was corrected; yolk of egg was prescribed daily. Four months later there was considerable regrowth of hair. The second analysis at this time showed a percentage of sulphur of 4.4, an increase of 0.5 per cent. Hydrolyzed wool was not administered.

In the second patient, another young woman, with a low sulphur content of hair, 3.8 per cent, loss of hair appeared after considerable mental stress and strain during which time weight was lost; animal proteins were eaten daily. Three months after the first analysis there was considerable regrowth of hair, and a second analysis showed a percentage of sulphur of 4.5, an increase of 0.6 per cent. Hydrolyzed wool was not prescribed. Treatment consisted of the application of a stimulating lotion, ultraviolet exposure and measures to improve the state of health.

A second analysis of hair for the percentage of sulphur was made in two patients in this group after hydrolyzed wool therapy. These patients, who were young men with alopecia prematura, showed an increase in the percentage of sulphur of 0.5. There was, however, no clinical improvement.

Hair of patients with pellagra was included in this study, since the etiologic factor in this disease probably concerns a deficiency of amino-acids. Moreover, Smith [43] reviewed evidence which suggested that an inadequate supply of sulphur as cystine is an important cause of pellagra and that the abnormal metabolism of sulphur is an important feature of pellagra. Our purpose was to determine whether a dietary deficiency was associated with a low sulphur (cystine) content of hair. At the time of our study, the hair of only one patient with endemic pellagra was obtainable (from Dr. Ralph Hopkins of New Orleans). The

43. Smith, J. H.: The Influence of Solar Rays on Metabolism, Arch. Int. Med. **48**:907 (Nov.) 1931.

percentage of sulphur in this specimen was 4.2. Five specimens of hair were examined from patients with pellagra, experimentally produced. The average percentage of sulphur in this group was normal, i. e., 4.5. These specimens were obtained through the courtesy of Dr. G. A. Wheeler, United States Public Health Service. The diet [44] employed in producing pellagra in these patients consisted essentially of corn meal, peas, bread and cane syrup.

In order to correlate the sulphur content of hair in patients receiving an inadequate diet, we examined hair from two patients with inoperable gastric cancer. These patients had lost considerable weight; a liquid diet was given but was not completely retained. Neither patient had loss of hair. In one, a man with thin hair who had been partly bald for years, the percentage of sulphur was 4; in the other, a woman with gray but otherwise normal hair, the percentage of sulphur was 4.5.

The percentage of sulphur in the hair of three patients with seborrhea was normal; the average was 4.76 per cent.

In three different patients in each of the following groups with loss of hair accompanying parturition, fever and secondary syphilis, the percentage of sulphur in the hair was generally normal. An exception was in a patient with secondary syphilis, who had a pronounced loss of hair, the percentage being 4.1.

Percentages of sulphur of 5 and above were obtained in a total of eight specimens in the entire series; in all but three, these specimens were obtained from patients to whom hydrolyzed wool was being administered. In all patients in whom a second analysis of hair was made, after hydrolyzed wool therapy, the percentage of sulphur was increased. Such an increase ranged from 0.4 to 0.6 per cent.

Growth of hair on the face or body was not unfavorably affected in any of the patients to whom hydrolyzed wool was administered. The preparation apparently acted as a tonic to a few of the children in the series, since, after taking it, their appetite was increased and they gained in weight.

P-THIOCRESOL IN PROMOTING GROWTH OF HAIR

Hammett, Reimann and their co-workers [45] have demonstrated that SH or the sulphhydryl group is stimulative specifically of cell multiplication and that the partially oxidized derivatives thereof are retardative. In their work, p-thiocresol was employed as the sulphhydryl-containing compound.

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44. Walker, N. P., and Wheeler, G. A.: Influence on Epilepsy of a Diet Low in the Pellagra-Preventive Factor, Pub. Health Rep. **46**:851, 1931.

45. Hammett, F. S., and Reimann, S. P.: Cell Proliferation Response to Sulfhydryl in Mammals, J. Exper. Med. **50**:445, 1929; The Influence of Sulfhydryl and Sulfoxide on Gross Regeneration in the Hermit Crab, Protoplasma **13**:261, 1931.

The major constituent of hair protein is cystine, a sulphhydryl-containing compound which is concerned in the growth of hair. Hammett and Reimann's observations suggested to us the local application of p-thiocresol to stimulate the growth of hair.

Laboratory Studies.—The following study was conducted to determine the value of p-thiocresol in stimulating the regrowth of hair in rabbits. Eight rabbits were employed. All were housed under the same conditions and maintained on the same diet. The hair on one half of one side of each animal was removed by the application of barium sulphide. Two animals had no further treatment. The bald areas on two animals were treated by the daily application of ultraviolet rays (air-cooled mercury quartz lamp). The dose was an erythema dose to the human skin. To the bald areas on two animals, p-thiocresol, 0.1 per cent, in olive oil, was applied daily by means of a medicine dropper. No mechanical friction was used. Since p-thiocresol is unstable, a fresh solution was made weekly. Two animals received ultraviolet treatment as well as applications of p-thiocresol. The experiment was continued for one month. There was no evidence that p-thiocresol stimulated the regrowth of hair. More accurate experimentation was deemed unnecessary. Ultraviolet rays appeared to be effective in stimulating regrowth.

Clinical Studies.—Patients with alopecia areata were treated. P-thiocresol, 0.1 per cent in olive oil, was applied daily to the bald areas by means of a medicine dropper without friction. Fresh solutions of the preparation were made weekly. Such treatment was carried out for four weeks. In some patients there was no regrowth of hair; in others, hair regrew. Regrowth in these patients was not striking; it compared to the regrowth that at times occurs in patients with alopecia who have received no treatment.

From these laboratory and clinical studies it is concluded that the local application of p-thiocresol is ineffective in stimulating the regrowth of hair.

NOTE.—Since writing this report we observed another favorable result in the treatment of a boy, aged 12, with alopecia areata totalis of two years' duration. Two weeks after the administration of hydrolyzed wool, hair was apparent on the scalp. After three months' administration, hair covered the entire scalp, but it was not a full growth. Hair appeared elsewhere.

COMMENT

It is apparent from the results of our studies of the sulphur content in fifty-three specimens of hair from forty-six different patients, that loss of hair is not necessarily associated with a low percentage of sulphur, and, conversely, it would appear that the metabolism of sulphur

(cystine) is not exclusively concerned in the cause of loss of hair. The metabolism of sulphur (cystine) is doubtless one phase only of the mechanism of the growth and the loss of hair. This mechanism apparently involves an interplay of other factors, notably, the endocrine glands and the sympathetic nervous system.

From our results it seems that it is possible to increase the sulphur content of hair by the administration of hydrolyzed wool, but that such an increase may or may not be accompanied by an increased growth of hair. It further appears that in loss of hair in which the sulphur content is abnormally low, an increase of sulphur is accompanied by an increased growth.

Dietary deficiency as a cause of loss of hair is more apparent in laboratory animals than in man. In a clinical visualization of the causes of loss of hair in man, dietary deficiency is not conspicuous; for example, loss of hair is not seen in starvation, cachexia or diseases attributed to amino-acid deficiency, notably, pellagra. It should be recalled, however, that in laboratory experimentation, in order to produce loss of hair, it is necessary to maintain animals for months on a low sulphur-containing diet. Moreover, hair in proportion to body weight is far greater in animals than in man.

Consistent with the foregoing facts, Prof. William Lentz of the Veterinary School, University of Pennsylvania, informed us that improper diet is a conspicuous cause of loss of hair in dogs.

Our studies do not suggest a disturbance of sulphur metabolism as a cause of loss of hair in alopecia areata, following parturition or fever or accompanying seborrhea and secondary syphilis. There is more evidence that such disturbance is operative in loss of hair attributed to causes other than the foregoing.

On the whole, it does not appear that disturbance of sulphur metabolism is a frequent cause of loss of hair; there is perhaps more evidence pointing to the sympathetic nervous system as a more important factor. On the other hand, our observations of a low sulphur content in abnormal states of nails and somewhat more favorable results in therapy of such with hydrolyzed wool than that obtained in patients with loss of hair suggest disturbance of sulphur metabolism as a more frequent factor in disorders of the nails of systemic origin. A clinical correlation of this is the fact that sudden loss of nails does not occur, comparable to the sudden loss of hair following mental stress and strain.

Metabolism of sulphur [46] (cystine) and sulphur content of food, so far as they pertain to the growth of hair and a possible rôle in the

46. Kahn, M., and Goodrich, F. G.: Sulfur Metabolism, Philadelphia, Lea & Febiger, 1926. Lewis, H. B.: Sulfur Metabolism, Physiol. Rev. **4**:394, 1924.

loss of hair, are pertinent to the dermatologist, indeed to the veterinarian, and should be included in a consideration of loss of hair.

Therapy that influences the growth of hair and nails through internal administration is sounder in principle than therapy by local application of stimulating agencies as heretofore employed. The value of such treatment is controversial. It is to be recalled that Forster,[39] in well conducted experiments, failed to demonstrate any value in local application of a number of substances alleged to promote the growth of hair.

In a clinical study of loss of hair and of abnormalities of the nails, in order to promulgate therapeusis, it may be desirable to determine the sulphur content of these tissues. If the sulphur content is lower than normal, the administration of hydrolyzed wool or allied preparations and a diet high in sulphur would be indicated, rather than the routine prescription of such preparations.

SUMMARY

Keratin is the chief constituent of hair and nails. Since keratin has a high sulphur content in the form of the amino-acid cystine, it would appear that the metabolism of sulphur plays an important rôle in the development and growth of these tissues.

Reported studies of the cystine content of hair and other keratins were reviewed.

Reported studies of nutrition in laboratory animals show that there is a relationship of the protein content of the diet to the growth of hair. Production of hair is related to a diet containing the amino-acid cystine. Demands for protein (and cystine) for the growth of hair appear to be secondary in importance to the demands for the growth of the body with its more essential tissues. The addition of cystine to a diet the protein content of which was so low as to be the limiting factor in growth and was deficient in this amino-acid increased its value in the promotion of growth of hair in the albino rat. The production of a superkeratinized hair does not seem to result from the feeding of excessive amounts of cystine.

The literature was reviewed relative to the therapeutic use of keratin to promote the growth of human hair. The preparation proposed by Zuntz, a keratin prepared from horn, administered orally, and similar preparations known were discussed. Conflicting reports relative to the value of these preparations, administered orally, to promote the growth of human hair were reviewed.

The value of other agents locally applied in promoting the growth of hair was discussed.

The therapeutic use of keratin in the treatment of loss of hair in man was studied. The administration of cystine per se is not practicable in view of its expense. Of the available keratins from which to prepare cystine, wool was selected as the most preferable. Hydrolyzed wool as prepared is a dark brown solution containing 1.5 Gm. of cystine in 32 cc. and other amino-acids, indeed, all the primary constituents of wool that may be concerned in the growth of epidermal tissue containing keratin.

From laboratory studies it was concluded that hydrolyzed wool, administered orally, furnishes the requirements for the growth of hair in rabbits fed on a cystine-poor diet.

SH, or the sulphhydryl group, acts as a stimulant of cell multiplication. Cystine, a sulphhydryl-containing compound, is concerned in the growth of hair. A sulphhydryl-containing compound, p-thiocresol, was employed locally in an experimental study on rabbits and in patients with alopecia areata. Such applications were ineffective in stimulating the regrowth of hair.

Forty patients of both sexes and different ages, with loss of hair attributed to various causes, were given hydrolyzed wool. The preparation was administered by mouth and continued in the absence of other treatment for at least one month, and, in a number of cases, for three months or longer. Only two outstanding favorable results were obtained. Both patients had alopecia areata totalis, which existed for three years in one patient and for two years in the other. In other patients with alopecia areata totalis, no regrowth of hair occurred. The effectiveness of the preparation was doubtful in young men with alopecia prematura and in patients with thin and scanty hair associated with seborrheic eczema. In many patients with alopecia areata, the preparation was ineffective. In others with alopecia and in some patients with loss of hair attributable to other causes, hair regrew after the taking of hydrolyzed wool.

Study of the sulphur content of hair in conditions associated with loss of hair and of the effect of hydrolyzed wool therapy on this content were made.

The normal percentage of sulphur in hair was regarded to range from 4.5 to 5.2. From the results of this study, it appears that loss of hair is not necessarily associated with a low percentage of sulphur, and, conversely, it would seem that the metabolism of sulphur (cystine) is not exclusively concerned in the cause of loss of hair. It is possible to increase the sulphur content of hair by the administration of hydrolyzed wool, but such an increase may or may not be accompanied by an increased growth of hair. In loss of hair in which the sulphur content is abnormally low, an increase of sulphur is accompanied by an

increased growth. Dietary deficiency as a cause of loss of hair is more apparent in laboratory animals than in man. On the whole, it does not appear that a disturbance of sulphur metabolism is a frequent cause of loss of hair.

In a clinical study of loss of hair, in order to promulgate therapeusis, it is desirable to determine the sulphur content. If such content is lower than normal, the administration of hydrolyzed wool or allied preparations and a diet high in sulphur would be indicated, rather than the routine prescription of such preparations.

NOTE.—Since this report was written, du Vigneaud, Dorfmann and Loring published studies [47] in the direction of determining whether or not the dextro isomer form of cystine can be utilized for purposes of growth in lieu of the naturally occurring *b*-cystine. They demonstrated that *d*-cystine cannot be utilized for purposes of growth in lieu of *b*-cystine.

It is not possible to determine in what form cystine is present, whether *d*-cystine or *b*-cystine. *L*-cystine is formed in the beginning of hydrolysis; it requires prolonged heating with acid to produce appreciable amounts of *d*-cystine. Hydrolysis, therefore, should be discontinued after four hours.

2101 Pine Street.

1934 Spruce Street.

DISCUSSION

DR. HOWARD FOX, New York: The idea of Zuntz of Berlin that a preparation rich in cystine might promote growth of hair seems to have been reasonable. Such a preparation was marketed as a remedy to promote growth of hair, in 1920, I think. A few years later Dr. Sharlit, in our clinic, made some studies on this preparation. He found that it did increase the growth of hair, but that it did not cause growth of hair in follicles that had contained no hair. This preparation died a natural death, and nothing more has been heard about it.

Cystine is one of the foundation stones in the formation of keratin which forms the basis of the hair and nails. It would seem that there cannot be a great lack of cystine in the average person or there would be a deficiency of the horny layer of the skin. In some persons, however, there may be just enough cystine to supply the horny layer of the skin but not enough to supply the hair and nails. It might be proper to feed such persons cystine. In persons with a well balanced diet, the question would not be to supply more cystine but in some way to direct the cystine to the tissues like the hair and the nails. How this could be done I do not know. Brown and Klauder in their interesting piece of work have shown that their preparation has caused the growth of hair in animals, though in human beings it has not been satisfactory.

DR. FRED D. WEIDMAN, Philadelphia: I can imagine two ways in which a sulphur compound would play a rôle in the nutrition and maintenance of hair. One has interested me today, i. e., in supplying a deficiency. The other is in the way of a stimulus to the hair bulb, to stimulate the growth of hair. Reimann [48] and

47. du Vigneaud, V.; Dorfmann, R., and Loring, H. S.: J. Biol. Chem. **98**:577 (Nov.) 1932.

48. Reimann, S. P., and Hammett, F. S.: The Proliferative Reaction of the Skin to Sulfhydryl and Its Biological Significance, Protoplasma **13**:331, 1931.

his associates have recently been elaborating sulphhydryl compounds for accelerating the healing of wounds. Cystine will stimulate hyperplasia of epithelial cells, and is a sulphhydryl compound. Perhaps these items may be made to fit in with the subject of increased growth of hair, if, as and when referable to cystine.

Dr. Earl D. Osborne, Buffalo: I should like to ask two questions. Has Dr. Klauder made any examination of the hair for sulphur content in conditions producing alopecia, following various fevers, pneumonia, toxemias and other disorders? What is the effect on the metabolism of sulphur in the human body of the fever or the toxemia?

Dr. Joseph V. Klauder, Philadelphia: Relative to the remarks of Dr. Weidman, I did not have time to mention our studies with p-thiocresol as recorded in the paper. I saw one of the histologic slides in Hammett and Reimann's study in which a hair follicle apparently formed following the application of p-thiocresol to the skin of a white mouse. This suggested to us the local application of the drug to areas of alopecia areata. Such applications of the drug were ineffective.

In view of apparently favorable results in at least two cases of alopecia totalis, I think that the administration of hydrolyzed wool to such patients is worthy of trial. I intend to employ hydrolyzed wool in the treatment of patients in whom examination of the hair shows an abnormally low sulphur content. Its use is worthy of a trial in patients with abnormalities of the hair which were not included in our series, for example, trichorrhexis nodosa. Such patients were not available during the time of our study.

Our results in patients with diseases of the nails will be published in a separate report. The use of hydrolyzed wool in the treatment of diseases of the nails has been somewhat more favorable than in the treatment of patients with loss of hair.

The question of Dr. Osborne is answered in the paper. In a small series of patients with loss of hair attributed to seborrhea, to secondary syphilis and to loss of hair after fever, the sulphur content of the hair is normal. I am not acquainted with any data in the direction of showing a disturbance of sulphur metabolism in patients with fever.

Dr. Frank W. Cregor, Indianapolis: I only wish to state that the United States Department of Agriculture has persistently refused to allow the entrance of "humagsolan" into this country.

LINGUAL PURPURA

REPORT OF A CASE

HERBERT RATTNER, M.D.
CHICAGO

The purpose in this paper is to report a case of lingual purpura in which the lesions of the tongue were so unusual as to make a clinical picture with which I was entirely unfamiliar. Dr. William Allen Pusey and Dr. L. F. Weber examined the patient with me, and they, too, had never seen a similar case.

REPORT OF CASE

L. A., a mulatto, aged 20, a premedical student, was referred by his physician to the dermatologic clinic of the Post-Graduate Hospital. He gave the following history: He awoke in the morning to find that his sputum was blood-stained, and, on examining his mouth, he found a blood blister on the tip of his tongue and another one on the inner surface of the lower lip, which had ruptured. That afternoon, several more lesions appeared on the tongue; and, on the following day, when he appeared at the clinic, there were about twenty lesions in the mouth distributed on the sides of the tongue, the buccal mucous membranes and the inner surface of the lower lip and on the pharynx. There were no subjective or constitutional symptoms. The patient felt no discomfort. He had never had a similar experience, and he had not used any irritants or drugs that might be responsible for the lesions. He noted particularly that there was no apparent change in the color of the urine or stool.

The lesions on the tongue were conspicuous and presented a striking picture. They consisted of thin-walled vesicles filled with blood. The vesicles were dark red to purplish, and they were distributed bilaterally and symmetrically on the edges of the tongue. Each lesion was the size of a pea, irregularly round with a rounded top. The lesions were raised appreciably from the surface, springing from an apparently normal base. There was no surrounding halo of inflammation. The lesions were discrete, and they were practically of uniform size; they felt firm, and they were neither tender nor painful. When a lesion was punctured, there was a discharge of dark, bloody serum.

On the buccal surfaces of the cheeks and lips, the lesions had ruptured, leaving flat, purple-stained areas, from which the color did not fade on pressure. The lesions in the pharynx consisted of several tiny, pinhead-sized petechial spots arranged symmetrically. There were no other lesions in the mouth.

General examination revealed lesions also on the shoulders, the legs and on the left forearm. On the shoulders and above the ankles there were patches made up of pinhead-sized follicular petechial spots. These lesions were macular and reddish brown. The patches were symmetrical, irregular and rather sharply defined, and they were not associated with subjective sensations. There was a solitary lesion on the left forearm, which differed slightly from the others, and which was probably the beginning of the condition. It was a bluish, edematous, rounded papule, three-eighths inch (9 mm.) in diameter and raised from the surface of the skin. Surrounding this there was a ring of pinhead-sized petechial lesions similar to those on the legs. The central papular lesion was the result of an insect bite. The patient recalled that on the day prior to the appearance of the lesions in the mouth, while

he was working with his sleeves rolled up, he was bitten on the forearm by an insect. He remembered this incident vividly, for, though the sensation lasted only a moment, it was very painful. Within a few minutes the area of the bite "raised up like a hive," and after several hours it turned red and gradually blue. It itched most of the day until the swelling had receded. On the following day, the surrounding petechial lesions made their appearance. Other than these, there were no findings.

The patient, in short, presented purpuric lesions in the mouth and on the shoulders and legs, all of which spread within twenty-four hours following an insect bite. The lesions of the skin were typical purpuric macular lesions. Those in the mouth were most unusual. None of the lesions caused discomfort. When the patient was seen again in three days, those in the mouth had disappeared, leaving no traces, and those on the skin were undergoing resolution.

Photograph of tongue, showing purpuric lesions.

The diagnosis was undoubtedly that of hemorrhage into the mucous membranes and skin—a symptomatic toxic purpura. It is likely that the toxin was provided by the insect, a situation analogous to the toxic purpuras produced from venomous snake bites. The sequence of events was so sharp as to make this explanation plausible. The uncommon feature was the clinical picture in the mouth. The large number of lesions on the tongue, their color, their discrete character, their symmetrical distribution, the lack of symptoms, and the thin-walled vesicular lesions filled with blood, which made them conspicuous, altogether made a unique and interesting clinical entity.

SUMMARY

A young man was bitten on the forearm by an insect. The following day, purpuric lesions developed on the tongue, buccal mucous membranes, lips, pharynx, shoulders and legs. The lesions on the tongue were vesicular. The case is reported because of the unusual clinical picture produced by the oral lesions. Its counterpart had never been seen by several experienced observers.

7 West Madison Street.

TRICHOPHYTOSIS, INCLUDING ONYCHOMYCOSIS UNIVERSALIS, SIMULATING TINEA IMBRICATA

REPORT OF AN UNUSUALLY EXTENSIVE CASE

HERMAN E. KITTREDGE, M.D.

Dermatologist to Saint Elizabeth's Hospital; Dermatologist to Providence Hospital; Associate Dermatologist to the Central Dispensary and Emergency Hospital

WASHINGTON, D. C.

Realizing the greater luxuriance of all forms of plant life in the tropics, it is not difficult to understand an analogy between the tinea imbricata of those regions and widespread dermatophytosis (of tropical origin) in the north. As early as 1855 Bärensprung [1] insisted that tinea circinata was etiologically identical with eczema marginatum, and in 1878 Tillbury Fox [2] stated that "some forty and more medical men, practising in tropical parts, . . . entirely concur in the view that eczema marginatum and the oriental phase of ringworm known as Indian, Chinese," etc., that is, tinea imbricata, "are one and the same disease."

That Bärensprung and Fox did not have the advantage of the later clarifying mycologic work of Castellani and Sabouraud on the epidermophytons and of Castellani on the endodermophytons is beside the mark: it does not detract from the significance of the view of the "forty and more medical men" on the point that I wish to emphasize. That point is: In a temperate climate like that of North America, an extensive trichophytic eruption of tropical origin may constitute a clinical analog of the tinea imbricata of the tropics. Such is the case reported in this paper.

Read in part before the Medical Society of the District of Columbia, Oct. 5, 1927.

From the dermatologic service of Dr. Herman E. Kittredge, Saint Elizabeth's Hospital.

The patient in the case reported was shown (as having onychomycosis universalis) before the Baltimore-Washington Dermatological Society in 1928.

1. Bärensprung, quoted by Bulkley, L. Duncan: On the So-Called Eczema Marginatum of Hebra (Tinea Trichophytina Cruris), As Observed in America: A Clinical Study, Chicago M. J. **35**:449 (Nov.) 1877.

2. Fox, Tillbury: On So-Called Eczema Marginatum, Arch. Dermat. **4**:291, 1878.

CHARACTER AND EXTENT OF ORDINARY RINGWORM

It is the general impression that ringworm of the body manifests itself, in a great majority of cases, by the appearance of one or several —at most, a dozen—small, nonelevated or slightly elevated, circinate or irregular, erythematous, scaly spots or patches. The irregular ones usually maintain a uniform scaliness; the circinate ones clear, or partially clear, in the center, while advancing at the periphery to form rings, single or concentric, and occasionally coalesce with adjacent lesions into plaques with polycyclic borders. Shoemaker,[3] Gottheil,[4] Stelwagon and Gaskill,[5] Hartzell,[6] Macleod,[7] Sutton,[8] Whitfield,[9] Pusey,[10] MacKenna,[11] Knowles,[12] Hazen,[13] Low,[14] Ormsby,[15] Riehl and Zumbusch,[16] and Strickler [17] are in substantial accord with this description.

TRICHOPHYTOSIS VERSUS EPIDERMOPHYTOSIS IN DERMATOPHYTOSIS

In this paper, trichophytosis denotes infection by a trichophyton, and epidermophytosis, infection by an epidermophyton, while dermatophytosis "includes all those superficial fungous infections of the gla-

3. Shoemaker, John V.: A Practical Treatise on Diseases of the Skin, ed. 3, New York, D. Appleton and Company, 1898, p. 755.

4. Gottheil, William S.: Illustrated Skin Diseases, ed. 2, New York, E. B. Treat & Company, 1906, p. 108.

5. Stelwagon, Henry W., and Gaskill, Henry Kennedy: A Treatise on Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1923, p. 1161.

6. Hartzell, Milton B.: Diseases of the Skin, ed. 2, Philadelphia, J. B. Lippincott Company, 1919, p. 411.

7. Macleod, J. M. H.: Diseases of the Skin, London, H. K. Lewis & Co., Ltd., 1920, p. 384.

8. Sutton, Richard L.: Diseases of the Skin, ed. 8, St. Louis, C. V. Mosby Company, 1931, p. 1182.

9. Whitfield, Arthur: A Handbook of Skin Diseases, ed. 2, London, Edward Arnold & Co., 1921, p. 52.

10. Pusey, William Allen: The Principles and Practice of Dermatology, ed. 4, New York, D. Appleton and Company, 1924, p. 769.

11. MacKenna, Robert W.: Diseases of the Skin, New York, William Wood & Company, 1923, p. 147.

12. Knowles, Frank Crozer: Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1923, p. 431.

13. Hazen, Henry H.: Diseases of the Skin, ed. 3, St. Louis, C. V. Mosby Company, 1927, p. 245.

14. Low, R. Cranston: The Common Diseases of the Skin, ed. 7, London, Oliver & Boyd, 1927, p. 57.

15. Ormsby, Oliver S.: A Practical Treatise on Diseases of the Skin, ed. 3 Philadelphia, Lea & Febiger, 1927, p. 946.

16. Riehl, G., and Zumbusch, Leo V.: Atlas of Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1925, pt. 1, p. 41.

17. Strickler, Albert: Textbook on Diseases of the Skin and Syphilis, Philadelphia, F. A. Davis Company, 1927, p. 425.

brous parts of the skin, particularly the intertriginous forms or those with intertriginous affinities" (Weidman).[18]

To demonstrate even approximately the parts played by the several genera and species of fungi in clinical dermatophytosis is, of course, the task of the mycologist. I do not entertain such an ambition or desire, but aim merely to indicate in a general way, in a few words, the evidently predominant rôle of the trichophytons, in comparison with the epidermophytons, in such unusually extensive examples of dermatophytosis as are presented in this paper. It is apparent that the rôles of these two principal actors have interchanged, in recent years, in the mycologic spotlight. For, in his earlier writings, Sabouraud taught that Epidermophyton inguinale produced not only all types of eczema marginatum, but most of the infections of the hands and the feet, and as late as 1920 Darier[19] stated: "It was formerly taught that the confluence of two or more lesions in trichophytosis may give rise to polycyclic spots or arabesques, and that a considerable portion of the integument may become invaded; in all probability many cases of this kind belong to the group of epidermophytosis." Since this was written the situation has been practically reversed. While it is now admitted that the epidermophyton may invade any part of the glabrous skin, the scalp, and even the nails, it is significant that 112 of the 114 generalized cases in Weidman's[18a] "Catalogue of Fungus Species in Epidermomycosis" were caused by a trichophyton, and only 2 by an epidermophyton. All of the 11 extensive, generalized and universal cutaneous cases and the 19 with involvement of the nails, which will be mentioned later, in which a fungus was culturally identified were caused by a trichophyton.

With reference to the etiology of dermatophytosis of the feet, Weidman,[18a] commenting on his "Catalogue," said:

> Doubtless the greatest surprise comes in respect to E. cruris. According to the reports of Sabouraud and Whitfield, this organism was the one to be expected most commonly between the toes. . . . It now develops that Trichophyton interdigitale is the most common in the northern states, whereas Trichophyton rubrum and interdigitale are the commonest in the southern states, in Manchuria and in Japan.

Ballagi,[20] in Budapest, in a series of 800 cultures, grew an epidermophyton (E. inguinale) only 63 times. My case qualifies as one of trichophytosis, under the foregoing postulates, as a trichophyton was identified in it.

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18. (*a*) Weidman, Fred D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927; (*b*) Dermatophytosis: The Newer Ringworm, J. A. M. A. **90**:499 (Feb. 18) 1928.

19. Darier, J.: A Text-Book of Dermatology, Edited with Notes by S. Pollitzer, ed. 2, Philadelphia, Lea & Febiger, 1920, p. 524.

20. Ballagi, quoted by Mitchell, James Herbert: Need for Research in the Treatment of Epidermophytosis, J. A. M. A. **89**:421 (Aug. 6) 1927.

EXTENSIVE, GENERALIZED AND UNIVERSAL RINGWORM

Apparently only 10 cases have been recorded in English.

The case of Nettleship [21] (1875) was the first sufficiently extensive to warrant inclusion in the group. In this case, a girl, aged 4½ years, exhibited at least 40 patches which appeared with unusual rapidity on the face, neck, backs of the forearms, fronts of the knees and other parts of the limbs.

Elsner [22] (1891) reported a universal case, that of a man, aged 24, who had a "parasitic eczema in which the parasite became engrafted upon the finger-nails, by scratching, no doubt, and upon the toe-nails, by simple extension or contact with stockings," etc. "The eczema of the body . . . merged into a universal dermatitis, with free exfoliation . . . and . . . agonizing itching. . . ." The extent of the onychomycosis (which will be referred to again) was not definitely indicated.

Cantrell [23] (1896) described an extensive tinea cruris that dipped down below the pubes and eventually invaded the entire abdomen and part of the chest.

Gottheil [4] (1906) recorded an extensive case of trichophytosis involving the genitocrural, epigastric, pectoral, axillary, infra-axillary and iliac regions.

Ohmann-Dumesnil [24] (1906) reported an extensive case with disseminated individual lesions on the legs, thighs, abdomen, chest and arms. In some places, scalloped and circular figures were formed.

Sequeira [25] (1906) recorded a generalized case of trichophytosis, in a boy of 14 years, involving the entire trunk, the dorsa of the feet, parts of the arms, the hands and all of the finger-nails. There was ulceration of the umbilicus.

Freeman [26] (1907) described a universal case of tinea tropica circinata in a marine.

> In October . . . while serving in and about Cuba, a skin disease like itch appeared at the interdigital spaces. This, however, soon disappeared; . . . in

21. Nettleship, Edward: Tinea Circinata Occurring in Very Numerous Patches, and with Unusual Rapidity, Brit. M. J. **2**:672, 1875.

22. Elsner, F. W.: Two Cases of Fungus Disease of the Nails (Onychomycosis)—(1) Tinea Favosa Unguium; (2) Tinea Trichophytina Unguium et Universalis, Australian M. J. **13**:479 (Oct. 15) 1891.

23. Cantrell, J. Abbott: An Extensive Case of Tinea Cruris, J. Cutan. Dis. **14**:104, 1896.

24. Ohmann-Dumesnil, A. H.: A Case of Disseminated Tinea Circinata Corporis, St. Louis M. & S. J. **90**:171 (April) 1906.

25. Sequeira, James H.: Extensive Ringworm with Ulceration of the Umbilicus, Brit. J. Dermat. **18**:269 (Aug.) 1906.

26. Freeman, G. F.: Tinea Tropica Circinata, U. S. Nav. M. Bull. **1**:27 (April) 1907.

November . . . at Norfolk, Va., the same lesions appeared on the legs and . . . abdomen; . . . the eruption included a variety of forms—erythematous, lichenoid, vesicular, circinate, etc. . . . Mycelia were found at the site of every variety of lesion; . . . the disease spread rapidly over the entire body [except the plantar and palmar surfaces and the head] after the patient had arrived in a cold climate [Portsmouth, N. H.] and was surrounded by good hygienic conditions. . . . The case . . . was exactly similar to many seen in tropical service, and was of interest as occurring in a cold climate. . . .

In 1909 Sequeira [27] showed a patient with a generalized case in which the eruption extended from the neck over the whole trunk to the thighs, and down the arms to the hands. The affected areas were scaly, and had a sharply marked margin. The left ear was involved. All the nails of the hands were diseased.

Little [28] (1915) reported a generalized case of tinea in a soldier from West Africa. There were large ringed patches and eczematoid surfaces. The eruption began in the groin and spread to the abdomen, pubes, scrotum, thighs, legs, dorsa of the feet, clefts between the toes, sides of the chest, sacral and interscapular regions, nape of the neck, left side of the face, axillae, forearms and backs of the hands.

Hartzell [29] (1919) described an extensive case of tinea covering almost the entire deltoid region and a large part of the right half of the trunk. The eruption was papular and nodular and, apart from some secondary excoriations, resembled considerably a slowly spreading nodular syphiloderm.

RINGWORM OF THE NAILS

Since one of the major features giving uniqueness to the case herein reported is the universal involvement of the nails, it seems relevant to review the salient points and the extensive cases in the English literature of that phase of the subject.

Frequency.—The majority of authors consulted who have definitely expressed themselves on the point have hitherto agreed that ringworm of the nails is rare among diseases of the skin and extremely rare among diseases in general. To quote Grindon: [30]

Onychomycosis is extremely rare. . . . Most observers proclaim the extreme rarity of the affection. Thus Bulkley reports four cases out of 10,000 of all dermatoses. Neither Crocker, out of 12,000 cases, nor McCall Anderson, out of

27. Sequeira, J. H.: Case of Extensive Ringworm of the Body and Limbs, Proc. Roy. Soc. Med. (Sect. Dermat.) **2**:1, 1909.

28. Little, E. G.: Proc. Roy. Soc. Med. (Sect. Dermat.) **9**:55, 1915.

29. Hartzell, M. B.: Two Unusual Cases of Ringworm, One of Them Due to a Fungus (Trichophyton Rosaceum) Producing Pink Cultures, Arch. Dermat. & Syph. **1**:1 (Jan.) 1920.

30. Grindon, Joseph: J. Cutan. Dis. **19**:516 (Nov.) 1901.

11,000, among which were 178 trichophytoses, recorded a single instance. . . . Köbner, among 100 trichophytoses, found two of the nail.

Shoemaker [31] (1896) stated that the disease was almost unknown here. However, Foster [32] found a ratio of approximately 1:5,000 in over 500,000 immigrants examined at Ellis Island. In fourteen years, in France, Heller [33] saw only 2 cases in which he was able to demonstrate fungi. Sabouraud [34] stated that the disease is rare in Paris; Macleod,[35] that it is rare in England, and Hartzell [36] and Strickler,[37] that it is uncommon; Ormsby [38] considers it of great rarity. "On the other hand," again quoting Grindon,[30] "Pellizari had the astonishing proportion of 20 ungual cases out of 150 at all sites; and Arnozan and Dubreuilh record 11 out of 135 occurring among 37,000 dermatological patients." Hodges,[39] in a city of 12,000, placed the ratio at 1:500. White [40] stated that the condition is not rare, and that it occurred in 23 of his 1,013 patients. Hazen [41] said that it is not uncommon; Low,[42] that it is by no means uncommon, and Whitfield,[43] that it is probably more common than is generally supposed. Darier,[44] Stelwagon and Gaskill,[45] Pusey [46] and Knowles [47] do not express themselves concerning its frequency. It remained for Williams and Barthel [48] (1929) to present mycologic evidence at radical variance with all of the preceding opinions and statistics which place onychomycosis per se among the uncommon dermatoses. For, in every instance in a series of 40 cases

31. Shoemaker, John V.: Diseases of the Nails, Internat. Clin. **3**:332, 1896.

32. Foster, Milton H.: Favus and Ringworm of the Nails, J. A. M. A. **63**:640 (Aug. 22) 1914.

33. Heller, quoted by Lane, J. E.: Ringworm of the Hands and Feet, Boston M. & S. J. **174**:271 (Feb. 24) 1916.

34. Sabouraud, R.: Les teignes, Paris, Rueff & Cie, 1910.

35. Macleod (footnote 7, p. 417).

36. Hartzell (footnote 6, p. 639).

37. Strickler (footnote 17, p. 438).

38. Ormsby (footnote 15, p. 1205).

39. Hodges, Robert S.: Ringworm of the Nails, Arch. Dermat. & Syph. **4**:2 (July) 1921.

40. White, Charles J.: Fungus Diseases of the Skin, Arch. Dermat. & Syph. **15**:387 (April) 1927.

41. Hazen (footnote 13, p. 249).

42. Low (footnote 14, p. 61).

43. Whitfield (footnote 9, p. 69).

44. Darier (footnote 19, p. 433).

45. Stelwagon and Gaskill (footnote 5, p. 1008).

46. Pusey (footnote 10, p. 1202).

47. Knowles (footnote 12, p. 546).

48. Williams, Charles Mallory, and Barthel, Else A.: Tinea of the Toe-Nails as a Source of Reinfection in Tinea of the Feet, J. A. M. A. **93**:907 (Sept. 21) 1929.

of tinea pedis, these investigators recovered a fungus from the toe-nails. In all but 3 the fungus was identified as Trichophyton interdigitale. It should be noted, however, that these cases were practically asymptomatic: "The abnormality of the toe-nails was so slight that the patients were seldom aware of it, and an examining physician would ordinarily disregard it."

Extent and Distribution of Onychomycosis.—While Darier [44] and Ormsby [38] are noncommittal as to the anatomic location, Stelwagon and Gaskill,[45] Hartzell,[36] Macleod,[35] MacKenna [49] and Knowles [47] stated that the condition is more common on the hands than on the feet. In 16 cases, Low [50] found that the toe-nails were not affected. Only 4 of the writers consulted (two pairs of joint authors, McGlasson and Lehman [51] and Williams and Barthel [48]) found the disease more frequent on the feet. Since Williams and Barthel stated that their work proves definitely that tinea of the toe-nails is commonly associated with tinea of the feet, the most common of the dermatoses, the conclusion as to the anatomic location is obvious. My personal clinical observations in dispensary practice and, during a period of over five years, in a large institution where tinea, especially of the feet, is widespread, are in accord with that conclusion. In 5 of the 15 subuniversal cases reported, the hands were affected; in 2, the feet, and in 8, both the hands and the feet.

There is apparent accord among the majority of authors that the number of nails usually involved is small, from one to several. Stelwagon and Gaskill [45] and Knowles [47] say one or two; Pusey,[46] Sutton,[52] Hazen [41] and Greenwood and Swartz,[53] one or more; Hyde [54] says one or several; Darier,[44] several; Strickler,[37] Macleod [35] and MacKenna [49] say two or three, and Hartzell [36] and Ormsby,[38] one or several or all. Low,[50] in 16 cases, found from one to seven nails involved. He stated (elsewhere) [14] that the nails of all the fingers and thumbs may be affected, but that this condition is not common. Whitfield [43] and McGlasson and Lehman [51] are noncommittal.

Restricting this brief review of onychomycosis to ringworm proper, exclusive of tinea imbricata, in which many nails are often involved,

49. MacKenna (footnote 11, p. 153).

50. Low, R. Cranston: Fungus Infections of the Finger-Nails, Edinburgh M. J. **6**:121 (Feb.) 1911.

51. McGlasson, I. L., and Lehman, C. F.: Epidermophyton and Trichophyton Infections of the Skin, Texas State J. Med. **19**:626 (March) 1924.

52. Sutton (footnote 8, p. 1135).

53. Greenwood, Arthur M., and Swartz, Joseph H.: A Review of the Literature, Arch. Dermat. & Syph. **15**:404 (April) 1927.

54. Hyde, James Nevins: A Practical Treatise on Diseases of the Skin, Philadelphia, Lea Brothers & Company, 1893, p. 722.

there can be little doubt that invasion of all the toe-nails is frequent; that invasion of all the nails of the hands is infrequent, and that invasion of all twenty nails is among the rarest clinical phenomena in dermatology.

A careful search of the literature, in English, available in the Library of the Army Medical Museum reveals only 15 cases in which more than 7 and (as nearly as can be ascertained) less than 20 nails were involved. These cases were scattered over a period of thirty-two years. The reports follow, mostly in the numerical order of involvement, as accurately as can be judged: Sequeira [25] (1906) (2 cases), affecting all the nails of the fingers; MacKee,[55] for Fordyce (1915), all the nails of the fingers; Whitfield [56] (1908), 10 toe-nails; Sequeira [27] (1909), 10 nails of the hands; Shillitoe [57] (1910), 10 toe-nails: Waugh [58] (1920), most of the nails on the hands and a single toe-nail; Semon [59] (1923), 10 nails of the hands; Fox [60] (1921), 5 nails of one hand and 9 toe-nails. Hodges [39] (1921) reported 2 cases, one with 5 nails of one hand and 10 toe-nails infected and one with 5 nails of one hand and nearly all, if not all, of the toe-nails infected, the photograph presented being indistinct and the descriptive text inexplicit. Fox [61] (1920) reported a case involving 7 nails of the hands and 9 toe-nails, and Waugh [62] (1921), one in which most of the nails of the fingers and toes were affected. Elsner [22] (1891) failed to state the number of nails involved, but the inference is that many were affected; the case may have been a universal one. Macleod [63] (1922) mentioned a case occurring in a man from Java, in which all the nails of the hands and of the feet were infected; but no further report is available.

I have found definite reports of only 3 cases of onychomycosis universalis in English. The report of Little [64] (April, 1907) was the first. The patient, an omnibus driver, aged 40, had had the disease about fourteen years, and was supposed to have contracted it from mangy

55. MacKee: J. Cutan. Dis. **33**:211 (March) 1915.

56. Whitfield, Arthur: A Note on Some Unusual Cases of Trichophytic Infection, Lancet **2**:237, 1908.

57. Shillitoe, Arthur: Case of Ringworm of the Toe-Nails, Proc. Roy. Soc. Med. (Sect. Dermat.) **4**:151, 1910.

58. Waugh, J. F.: Trichophytosis, Arch. Dermat. & Syph. **3**:101 (Jan.) 1921.

59. Semon, H. C.: Tinea Unguium, Clin. J. **52**:233 (May 16) 1923.

60. Fox, Howard: Onychomycosis (Five Cases), Arch. Dermat. & Syph. **3**:85 (Jan.) 1921.

61. Fox, Howard: Tinea Unguium, Arch. Dermat. & Syph. **2**:249 (Aug.) 1920.

62. Waugh, J. F.: Onychomycosis, Arch. Dermat. & Syph. **3**:682 (May) 1921.

63. Macleod, J. M. H.: Brit. J. Dermat. **34**:208, 1922.

64. Little, E. G. Graham: Brit. J. Dermat. **19**:204, 1907.

horses. There was no concomitant ringworm of the body but there were some patches on the backs of the hands. Although typical hyphae were demonstrated in scrapings from 5 of the finger-nails, the organism was not culturally identified. About three months later (July, 1907), Ravogli [65] reported the second universal case; it was caused by Trichophyton megalosporon (endo-ectothrix). No mention was made of coexisting cutaneous lesions. Lancashire [66] (1912) reported the third case. The infection began in the toe-nails. There was no cutaneous eruption. The patient, a man aged 20 years, was supposed to have acquired the disease from infected cattle. Scrapings contained hyphae; an ectothrix grew on culture.[67]

The following is therefore the fourth case of onychomycosis universalis definitely reported in English and the third universal case so reported in which the fungus was cultured; it is the only universal case so reported associated with a cutaneous eruption of such uniformly homogeneous character and appearance as closely to simulate tropical ichthyosis (tinea imbricata).

REPORT OF CASE

History.—G. L. H., a white man, aged 52, a native of Florida, who had been employed in various occupations in several southern states, and who had served two enlistments in the army, reenlisted in the latter and was transferred to the Philippines. There (1903 to 1904) a psychosis developed. The patient was returned to the States, and he was admitted to Saint Elizabeth's Hospital in December, 1909.

In March, 1910, a Wassermann test of the blood was negative. On Oct. 14, 1914, general physical and neurologic examinations gave negative results.

Figure 1, taken on or soon after admission, that is, about eighteen years prior to the time when the patient came under my observation, shows the extent of the eruption at the time. It will be noted that the abdomen nearly as far upward as the navel, the legs to a point far below the knees and the arms from above the elbows to and including the wrists were already invaded. Whether the patient had received treatment that changed the appearance, or limited the extent, of the eruption when this photograph was taken is not known, and as his mental state (dementia praecox, deteriorated) was such that no information could be obtained from him, I am dependent on meager written records made from time to time by internists and psychiatrists for my ideas concerning the early history, nature and progress of the dermatosis.

The first definite notation concerning the dermatologic condition appears in his record under the date of Feb. 15, 1918: "Patient has a skin affection covering almost the entire body, especially the limbs. They are scaly, dry, and itchy." In January, 1921: "For some years, the patient has had an itching eczema, which spread from the groin up toward the abdomen, reaching the umbilicus, and down

65. Ravogli, A.: Onychomycosis Trichophytina, J. A. M. A. **49**:308 (July 27) 1907.

66. Lancashire, G. H.: Brit. J. Dermat. **24**:286 (Jan.) 1912.

67. Personal communication to the writer.

to the middle of the thighs." In November, 1921: "Marked trophic changes of the skin on the arms and from the waistline down. The trophic changes are in the nature of a rash, with no subjective symptoms." It is evident that the term "trophic" was used in the neurologic sense as best describing a cutaneous condition without dermatitis or other visible feature of the ordinary ringworms; that, in other words, simulation of tinea imbricata was already manifest. In January, 1922,

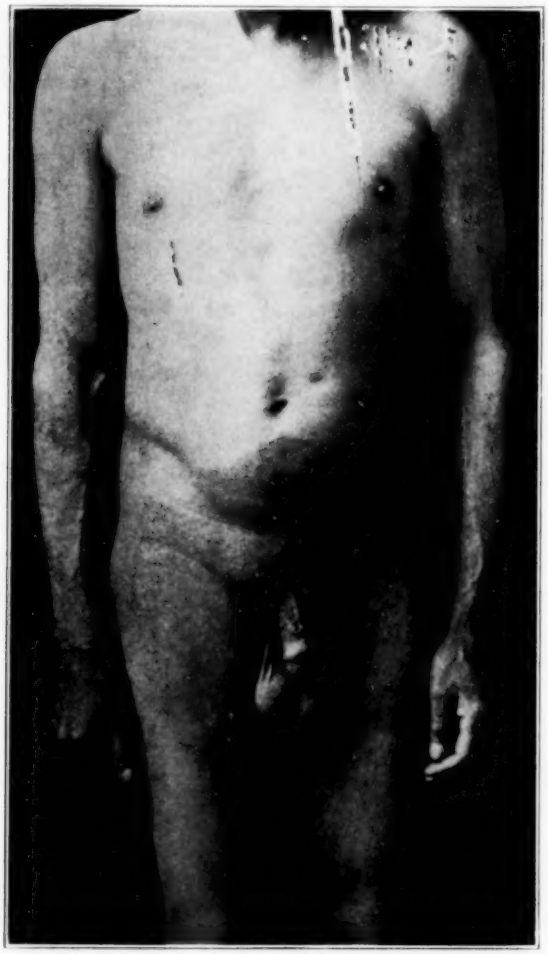

Fig. 1.—Photograph taken eighteen years before the patient came under my observation. Note involvement of the groins.

the rash over the same area is described as being of a dark chocolate color. In March, 1922, the patient was taken to the city to see the consulting dermatologist. Treatment was ineffective.

It should be stressed here, as an aid to a full realization of what a pitfall this case was and of what its general character and appearance were, that the consultant, though an exceptionally experienced and skilful dermatologic diagnostician,

made a diagnosis of ichthyosis. It is claimed that nearly every physician makes this error when he visits the far eastern tropics and is confronted with his first case of tropical ichthyosis, or tinea imbricata (Castellani and Chalmers[68]). For, as Henggeler, an authority on the latter disease, points out: "Occasionally the eruption becomes generalized, and the ringlike configuration is entirely lost. The ensuing clinical picture may be mistaken for that of a mild ichthyosis." It is not strange that the condition in the case reported passed unrecognized as ringworm for five years.

Frankly, when I made my first and rather hasty examination, I fell into almost the same trap as had my predecessor, as I proffered a tentative diagnosis of ichthyosis, with complicating eczema. Fortunately, my error was soon demonstrated by the action of a strongly keratolytic ointment which I applied, and which shortly disclosed, in a limited exfoliating area, several concentric rings, leading to immediate microscopic investigation.

In October, 1922, it was noted that "the patient has a very peculiar skin disease which covers a considerable body area, which is heavily pigmented. The finger-nails are also much hypertrophied." In 1926, the record concluded by stating that the pruritus was so violent that the patient had ceased scratching with his finger-nails and had substituted therefor the sole of his removed shoe.

Physical Examination.—When I made a careful examination of the patient, the clinical picture was that of a light chocolate-tinted, paper-like to horny, apparently imbricated scaliness, extending unbroken and uninterrupted by normal skin, from the middle of the trunk to the heels posteriorly, and from the upper third of the trunk to the feet anteriorly and laterally. This involvement included the axillae, the inguinogenital region and the entire upper extremities (fig 2), except a portion of the palms. The predominant feature was the coarse, brownish, ichthyotic appearance. The interdigital clefts of the feet were invaded; the soles were hyperkeratotic and scaly. Every nail of the hands and of the feet was dirty yellow, fissured, wormeaten in appearance and hypertrophied, the subungual spaces being choked with a granular substance, giving the nails an apparent total thickness of from ⅛ to ½ inch, 3 to 12 mm. (figs. 3, 4 and 6). Here and there the body, and the legs in particular, had the appearance of having been smeared with clay (fig. 2). The upper third of the chest, the upper half of the back, the neck, the face, the scalp and part of the palms were free from the condition. There was no dermatitis, save such as was secondary to the scratching induced by the unbearable pruritus that gives tinea imbricata one of its synonyms, Malabar itch.

Microscopic Examination.—The record of my direct microscopic examination of scrapings is incorporated in the mycologic report of Dr. Weidman. The blood picture showed: red cells; white cells, 2,600; polymorphonuclears, 43 per cent; lymphocytes, 37 per cent; eosinophils, 17 per cent; basophils, 2 per cent, and undifferentiated forms, 1 per cent.

Differential Diagnosis.—Ichthyosis was excluded by the results of the direct microscopic examination and by the action of parasiticidal and keratolytic applications, which soon revealed normal skin. Both trichophytosis and epidermophytosis were considered and excluded because of the morphology, appearance, distribution and extent of the eruption. Based on the history of residence in the Philippines, the dry, brownish, paper-like to horny apparently imbricated scaliness covering more than three fourths of the cutaneous surface but not involving the scalp, the

68. Castellani, Aldo, and Chalmers, Albert J.: Manual of Tropical Medicine, London, Baillière, Tindall & Cox, 1919, p. 2070.

Fig. 2.—Photograph taken shortly after the patient came under my observation. When this picture was taken, the original perfectly horizontal upper margin of the eruption, running sashlike across the chest, had been obliterated by treatment, as had the eruption on the right side. Note the involvement of the groins and the heaped-up, claylike formations on the left shin.

Fig. 3.—Photograph taken about four years after the patient came under my observation, showing the eight diseased finger-nails (onychomycosis).

absence of primary dermatitis, the violent itching, the heaped-up, claylike formations, especially about the legs (fig. 2), the involvement of the groins proper (figs. 1 and 2), the universal onychomycosis (figs. 3, 4 and 6) and the microscopic observations, including the pronounced eosinophilia, a tentative diagnosis of tinea imbricata was made.[69]

MYCOLOGIC REPORT

"*Microscopic Findings* [*Report by Dr. Kittredge*].—'Scrapings from the trunk, arms, legs and soles, soaked in a 15 per cent solution of potassium hydroxide, showed: (1) long, flat, rather narrow, branching, interlacing mycelial tubes, containing, at frequent intervals, small, round, refractive spores; (2) a fungus composed of very wide and very long segments, and of comparatively narrow and long segments, forming closed squares, oblongs and triangles; (3) oblong beaded or septate fungi, irregular in size, bearing a striking morphologic resemblance to Castellani's Endodermophyton indicum, one of the four organisms claimed by him to be the cause of tinea imbricata.

"'Scrapings taken separately from the finger-nails and the toe-nails, respectively, and treated for twenty-four hours in the same solution, showed: (1) numerous

Fig. 4.—Photograph taken about four years after the patient came under my observation. It shows the diseased thumb-nails (onychomycosis).

long, narrow to fairly wide, branching and interlacing hyphae, some of which were septate and spore-bearing; in other words, apparently the same organism that was found in the skin; (2) occasional beadlike strings of irregularly sized spores.

"'Microscopic examination of hairs from the invaded cutaneous surfaces gave negative results.'

"*Dextrose Agar Cultures* (*Pennsylvania Medium*).—Colonies two weeks old measured 1 inch (2.5 cm.) in diameter. The center was highly heaped-up, coarsely convoluted and more or less plateau-like; it sloped down suddenly to the margins. In the peripheral parts, there were from eight to ten coarse, irregular and fairly deep furrows. The margins were sharp. The surface was everywhere finely duveteuse and the texture strongly compact. The central parts were yellowish-white and the peripheral parts pink, with a faintly violaceous cast. The extreme marginal parts were dead white for a width of about 2 mm.

69. Scrapings were submitted to Dr. Fred D. Weidman, Laboratory of Dermatological Research, University of Pennsylvania, who conducted the cultural and determinative studies.

"Colonies six weeks old covered practically the entire agar slant (tubes 15 by 2.5 cm.). The central parts, again, were highly heaped up, but had now become closely convoluted and resembled a closely packed ball of earthworms. The rest of the colony was fairly voluminous, but it did not nearly reach the level of the central parts; it was a definitely luxuriant type of colony. The extreme periphery was thin and flat through only 5 or 6 mm., while the intermediate zone was more highly heaped up and was traversed by deep, irregular, but definitely radial, furrows.

"The surface was still duveteuse, but there was yet a suggestion of powderiness; one could envisage that there were spores intermixed with the mycelium, but at such a deep level that the overlying mycelium more or less masked them. All trace of pink coloration had disappeared; the surface ranged from a dirty gray to

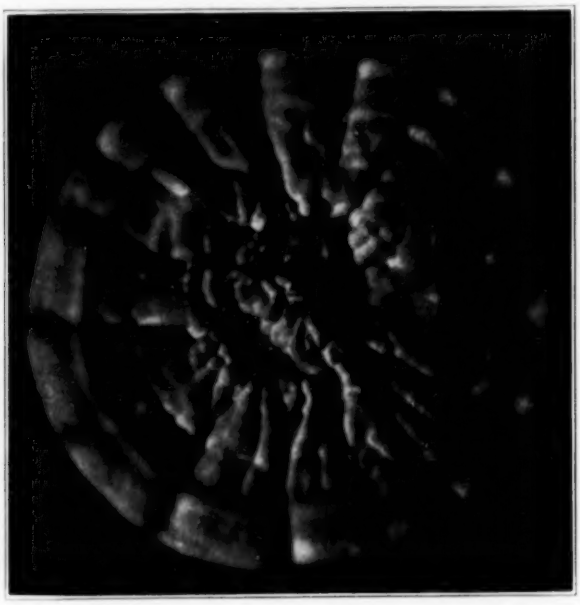

Fig. 5.—Giant colony one month old grown in Erlenmeyer flask on dextrose agar (Pennsylvania medium).

a dirty brownish gray, the latter color being more highly developed in the intermediate zone. The back of the colony was slightly discolored pale brown; the medium was slightly discolored brown, but turbid.

"*Hanging Drops: Dextrose Bouillon: Preparations Seventeen Days Old.*—The mycelium was of medium width, comparing in robustness with that of Trichophyton gypseum in general, and definitely segmented. Branchings occurred fairly frequently. The more coarse examples of hyphae had undergone extensive resorption of cytoplasm by this time. The more distal portions had developed thyrses sporiferes, but they were never lengthy, nor the beautiful symmetrical ones sometimes encountered in other species. Often there were intermediate arrangements between thyrses sporiferes and simple hyphae, with resorption of cytoplasm. In places there were accumulations of detached conidia.

"In addition to the broader hyphae, there were numerous and delicate non-segmented ones; many of them were strongly wavy, yet not sufficiently so to constitute spirals. They extended from the center of the colony to its periphery; less often they were arranged more circumferentially and interlaced with the radiate specimens. Only one or two definite chlamydospores were encountered; all were terminal. Many of the arthrospores that occurred in connection with the resorption of cytoplasm were so markedly swollen that they should be dignified as chlamydospores.

"There were a few examples of agglomerated chlamydospores which simulated organes nodulaires. At the present time they are not developed sufficiently to permit a final opinion.

"A definitely rose-red pigment was seen diffusely infiltrating certain individuals among all of the groups of fungus forms indicated—conidia, thyrses and both coarser and more delicate hyphae. No fuseaux or spirals could be found.

"*Determination of Species.*—The pink color attracts attention; but Tr. rosaceum may be eliminated on account of the development of convolutions and, particularly, because Dr. Kittredge's strain is not of niveum type. For the same reasons, Tr. vinosum may be eliminated. Tr. persicolor is definitely powdery and flat,

Fig. 6.—Photograph taken about four years after the patient came under my observation. It shows disease of all the toe-nails (onychomycosis), as well as cutaneous involvement of the interdigital clefts—after four years of more or less constant treatment.

never showing the convolutions which this species did. Tr. purpureum is a much more voluminuous colony from the start and does not become convoluted; furthermore, the back of the colony did not become pigmented in the way that Tr. purpureum does. Trichothecium roseum produces certain peculiarly shaped, gigantic spores which were not met in this strain.

"The hanging drop colonies could pass very well for a Tr. purpureum in which the elements had not proceeded to the full development of all the characters of that organism. This is particularly the case in view of the strong red pigmentation and the attempt at the development of thyrses sporiferes and spirals. All things considered, I regard this strain as one which is new to me at least, and one which has affinities with Tr. purpureum. However, there are such extremes in the test tubes between Tr. purpureum [70] and this strain that, in the present day sense, Dr. Kittredge's specimen should probably be regarded as a new species. This

70. Tr. purpureum is notorious for its vagaries; Ota has indicated this fact. It will doubtless develop into a group, with several varieties, in the way that Tr. interdigitale has.

should be deferred, however, in the present state of our knowledge of Tr. purpureum.

"Certainly the organism is not one of the endodermophytons described by Castellani. I have had the opportunity of examining species in this laboratory, and all of them have been of a definitely waxy type, like Tr. faviforme or Achorion schönleinii.

"Giant Colony on Dextrose Agar, One Month Old.—The colony (fig. 5) is 6.5 cm. in diameter and sharply marginated. A central zone comprises 80 per cent of the entire diameter and is sharply marked off from the peripheral margin by a shallow circular furrow. The immediate center of the colony is rather finely convoluted, while the peripheral parts are broken up by fairly numerous radial furrows. The latter, in turn, are occasionally divided transversely by shallow furrows. The marginal zone is also divided by radial furrows, but they are much shallower than the central ones. All of the radial furrows are rather uniformly spaced, giving a general aspect of orderliness and regularity to the entire colony (Tr. regulare).

"The texture of the colony is that of a compact duvet. For the most part it is grayish white with a faint yellowish undertone. Extremely faint pinkish nuances cropped out from place to place in the central zone, more particularly at the summits of the convolutions."

TREATMENT

One of the most effective applications for the eruption was that which has been found so useful in tinea imbricata—resorscin, 15 per cent, in compound tincture of benzoin. This was later followed, in resistant areas, by alcoholic solutions of salicylic acid, from 2 to 5 per cent, and by strongly keratolytic ointments. Whitfield's formula, in extra strengths, was fairly effective on the palms and soles. Because of the impracticability of carrying out systematic treatment, no serious attempt was made to do more than to hold the onychomycosis in check; and it is believed that subsequent reinfection from the nails was responsible for the fact that the skin was not quite clear at the time of the patient's death, from sudden cardiac failure, more than four years after treatment was instituted.

RECONCILIATION OF EXTENSIVE TRICHOPHYTOSIS AND CLINICAL TINEA IMBRICATA

Probably a majority of authors limit the size of the lesions in trichophytosis corporis to, say, ⅛ inch to 1 inch (3 mm. to 2 cm.) in diameter, if circinate, and to an equivalent area if irregular; but Hyde,[54] Ormsby [15] and Riehl and Zumbusch [16] stated that a patch, by peripheral extension, may reach a diameter of 6 inches (15 cm.). Several such patches, coalescing, give origin to polycyclic areas of arabesques, and they, in turn, to extensive homogeneous eruptions. The case of trichophytosis cruris presented by Gottheil,[4] in which coalescing multiple lesions covered the larger part of the anterolateral surfaces of the trunk, and which bore considerable resemblance to the case herein reported, is an example in point. It is not essential to the completeness of the analogy between tinea imbricata and trichophytosis that the latter should occur in concentric form; rather the opposite; for some cases of tinea imbricata are diffuse from the start, while in others "the eruption becomes

generalized and the ringlike configuration is entirely lost" (Henggeler). Between such a case and the one reported, the resemblance is so close as to render the two diseases clinically indistinguishable and to give ample support to the analog to which I have called attention. Indeed, a mere clinician is inclined to wonder whether some cases of tinea imbricata in the tropics are not caused by Trichophyton purpureum or related organisms.

SUMMARY

1. A case of unusually extensive ringworm of the body, probably of tropical origin, simulating tinea imbricata, and with associated onychomycosis universalis, is reported. It was caused by Trichophyton purpureum or a closely related organism.

2. It is possible that tinea imbricata is not an etiologic entity.

3. While extensive, generalized and even universal dermatophytosis has previously justified report, cases such as the one herewith reported are decidedly rare: simulation of tinea imbricata, together with onychomycosis affecting all twenty nails, makes it unique in the dermatologic literature of the English language.

412 Columbia Medical Building.

POSTOPERATIVE GANGRENOUS ULCER OF THE ABDOMINAL WALL

REPORT OF A CASE WITH SPECIAL NOTES ON TREATMENT

WERNER W. DUEMLING, M.S., M.D.
AND
RALPH W. ELSTON, A.B., M.D.
FORT WAYNE, IND.

During the past year there have been renewed interest and study in the subject of progressive gangrene of the skin following septic surgery. Since Cullen's [1] first reported case in 1924, a number of cases have appeared in the literature, some of which do not belong in this classification, but their study and presentation have done much to enlighten us on this subject. In 1931 Lynn [2] reported a case of postoperative gangrenous ulcer of the abdominal wall, and, in reviewing the literature, found twenty-one authentic cases. He included among these the case subsequently reported by Baker and Terry,[3] and noted this in his table of reported cases as "cured," but the authors stated that an endocarditis developed and the patient died. Lynn [2] also included a case of amebiasis cutis, reported by Cole and Heideman.[4] This case was seen and the diagnosis agreed to by Engman, who together with Heithaus [5] studied and reported three cases of amebic ulcer in 1919. The most recent contribution to this subject is that of J. Shelton Horsley,[6] who reported three cases, in all of which the patient recovered. One of these cases had been previously reported, and is included in Lynn's [2] twenty-one cases.

Almost all the cases have followed septic operations on the abdominal cavity, and have occurred in men. Exceptions to this are the cases reported by Borelli [7] (pelvic inflammatory disease), Brewer and

1. Cullen: Surg., Gynec. & Obst. **38**:579 (May) 1924.

2. Lynn, F. S.: Postoperative Gangrenous Ulcer of the Abdominal Wall, J. A. M. A. **97**:1597 (Nov. 28) 1931.

3. Baker, W. H., and Terry, C. C.: A Case of Postoperative Progressive Gangrene of the Skin, J. A. M. A. **98**:138 (Jan. 9) 1932.

4. Cole, W. H., and Heideman, M. L.: Amebic Ulcer of the Abdominal Wall Following Appendectomy with Drainage, J. A. M. A. **92**:537 (Feb. 16) 1929.

5. Engman and Heithaus: J. Cutan. Dis. **37**:715, 1919.

6. Horsley, J. S.: Certain Symbiotic Bacterial Infections Producing Gangrene, J. A. M. A. **98**:1425 (April 23) 1932.

7. Borelli: Gior. ital. d. mal. ven. **65**:326 (April) 1924.

Meleney [8] (abscess of the upper right quadrant, in a woman), Porter [9] (disease of the gallbladder, in a woman), Freeman [10] (disease of the gallbladder, in a woman) and Horsley [6] (extensive gangrene of the thigh and groin, extending up to the axilla and not starting from a wound of any kind). In the case reported here, the gangrenous ulceration followed an operation for a ruptured gastric ulcer.

REPORT OF CASE

History.—Mr. A. B., a white man, aged 42, married, with no children and with a wife living and well, was brought into the hospital with an acute surgical condition of the abdomen on the afternoon of Nov. 6, 1931. He was in shock, with severe abdominal pain, which the ordinary doses of morphine failed to relieve. For the past year he had suffered from indigestion of a vague type. On the morning that he became acutely ill, he had taken some soda, and later in the forenoon he drank considerable cider. He was in the field working, when at about 11 o'clock he was seized by a sudden acute cramplike abdominal pain which rendered him unconscious. He was found by a neighbor about two hours later. He vomited several times en route to the hospital.

Physical Examination.—The patient was tall and slender, with a very fair skin and flaming red hair, the type of person whose skin is sensitive to external irritation and infection. He was in shock. There was considerable oral sepsis, with numerous carious teeth and pyorrhea. The throat was injected. The heart and lungs were essentially normal. The abdomen was rigid and boardlike, and could not be satisfactorily palpated, because the slightest pressure elicited extreme tenderness. Rectal examination revealed nothing of note. The remainder of the examination yielded negative results. The temperature was 99.3 F., the pulse rate 122 and the respiratory rate 24. Urinalysis showed a trace of albumin, a few red and a few pus cells. A diagnosis of perforated gastric ulcer was made, and an immediate operation advised.

Operation.—An oblique high epigastric incision was made. There was a perforation nearly 1 cm. in diameter on the anterior surface of the stomach near the pyloris. The perforation was closed with chromic and silk catgut, with an implant of omentum over the closed area. One open tube was placed in the pelvis through a stab wound in the right loin, and one gauze wick and one Penrose tube drain were placed in the abdomen, coming out through the lower end of the incision.

Clinical Course and Treatment.—The patient was placed in Fowler's position, and nothing was given by mouth for twenty-four hours. At the end of the twenty-four hours, 1 drachm (3.8 Gm.) of sterile water was allowed every thirty minutes. This was increased to 1 ounce (28.3 Gm.) at the end of seventy-two hours, and then alternated with milk or broth. It is interesting to note that this patient, secretly, on the second day after his operation, drank the contents of his urinal as well as some water from a vase of flowers, which he was able to reach. Whether this had anything to do with his subsequent stormy course and abdominal gangrene is speculative. He got out of bed on two occasions during the first forty-eight hours, and was a very difficult patient to control. The gauze wick was removed on the fourth postoperative day. The soft rubber tube was removed on the fifth day, and the wound appeared fairly clean. The hard rubber tube was withdrawn an

8. Brewer and Meleney: Ann. Surg. **84**:438 (Sept.) 1926.
9. Porter, quoted by Lynn.[2]
10. Freeman: Ann. Surg. **92**:779 (Oct.) 1930.

inch each day until it was completely removed. On the seventh postoperative day, considerable seropurulent drainage was encountered from both the upper part of the wound and the stab wound, which had a fetid odor. This drainage persisted until the twelfth day, when it apparently subsided to some extent. The following day one could notice a slight ulceration developing at the site of the upper areas of drainage. Treatment of the wound with surgical solution of chlorinated soda was done twice daily, but the drainage and ulceration persisted. The necrotic area became larger, until nearly the whole incision was open and draining profusely, with definite necrotic borders. On the twenty-sixth postoperative day, ultraviolet irradiation was applied and given each day subsequently. The gangrenous ulceration progressed until there was an area the size of the palm with definite elevated

Fig. 1.—Photograph taken on the fortieth postoperative day, showing the extent of the lesion about twenty-six days after its first appearance.

edges, surrounded by a bright reddish-purple zone. On the thirty-sixth postoperative day, a bacteriophage dressing was applied. The ulceration spread rapidly, crusting in some areas and extending at the margins, until the larger part of the abdominal wall, down to the muscle layers, was involved.

On the fortieth postoperative day, the ulcer of the lower abdominal wall was about the size of an ordinary dinner plate (fig. 1). It extended down to the abdominal muscles; the base was clean, with small areas of epithelium scattered throughout. The upper right and entire left border was surrounded by a sharply demarcated dusky zone of erythema, with a lighter zone of redness about this, gradually fading out to normal skin. The lower right border was sloping in type and clean. In part the border was made up of a yellowish-brown undermined slough.

The patient's general condition was only fair. He had lost much weight, and had a moderately septic temperature. Cultures made at this time revealed a streptococcus, Staphylococcus aureus and a gram-negative bacillus. On numerous examinations the urine was sugar-free, and the Wassermann and Kahn tests were negative. Beginning on this fortieth postoperative day, continuous wet potassium permanganate packs were applied. One week later, the advancing and sloughing border was removed by actual cautery, according to the technic illustrated by Lynn.[2] After the cauterization the potassium permanganate packs were continued for one week. After the sloughs from the cauterization came away, a clean granulating surface remained. Until the cauterization the patient complained of intense burning pain, which was entirely relieved by this procedure. However, changing

Fig. 2.—Recurrences at the upper right border, which were arrested by infiltration with bacteriophage.

the dressings twice daily was still a painful ordeal, so strips of gauze impregnated with oxyquinoline sulphate and scarlet red ointment were applied directly to the area involved, using the formula and technic recommended by Bettman.[11] This was a new procedure for us, as we had previously employed the usual skin graft methods. Within ten days from the time the oxyquinoline sulphate and scarlet red were applied, the infection had practically cleared up, and the greater part of the area was already epithelized over. One week later, that is, on about the sixtieth postoperative day, a small area on the upper border began to slough again, and this area was again removed by cautery, followed by potassium permanganate packs. Apparently we did not go quite far enough back into normal tissue, as this area

11. Bettman, A. G.: A Simple Technic for Promoting Epithelization and Protecting Skin Grafts, J. A. M. A. **97**:1879 (Dec. 19) 1931.

alone persisted. Accordingly, two weeks later a second cauterization was done. For the next two days, the entire wound was dressed with packs moistened with physiologic solution of sodium chloride, following which the oxyquinoline sulphate and scarlet red ointment were again applied. The ulcerating area was apparently now well under control and practically epithelized over, except at the upper right margin. However, on the one hundred and tenth postoperative day, there was a small recurrence at the upper right border, which extended over the margin of the lower rib nearly to the nipple (fig. 2). A new procedure was employed. The skin and subcutaneous tissue beneath and ahead of the advancing border were infiltrated with 5 cc. of bacteriophage (the staphylococcus and colon bacillus). Following this the patient had a chill and the temperature went to 103 F. This infiltration was repeated at five day intervals for a total of three times, each general reaction becoming less severe. The remainder of the area was kept covered with the oxyquinoline sulphate and scarlet red dressings. From the time of the first infiltration, the progress of the recurrence was checked. Gradually the erythema faded, the pain ceased and the necrotic tissue sloughed out, leaving a clean base which healed. At the same time a small abscess formed along the line of the old incision, through which a small piece of silk suture was extruded; after this the area cleared up spontaneously. On the one hundred and twenty-sixth day, or slightly over four months from the date of operation, and about three and one half months from the onset of the gangrene of the abdomen, the lesion was arrested. There remained on this date only two small granulating areas, each about the size of a 5 cent piece. Within one week the lesion had entirely healed, and the patient was discharged from the hospital. The wound was completely epithelized over, without the aid of skin grafts, and there was very little contracture of the scar.

ETIOLOGY

In the cases reported in which bacteriologic studies have been made, one is struck by the fact that there seems to be no one causative organism. Cullen [1] found a streptococcus; Lynn,[2] a streptococcus, Staphylococcus aureus and a gram-negative bacillus. Freeman [10] found a "confusing multitude of micro-organisms," while Alexander [12] reported a staphylococcus, Micrococcus buccalis, Streptococcus haemolyticus and Micrococcus liquefaciens. In Horsley's [6] series of three cases, case 1 showed streptococci, gram-negative bacilli, gram-positive cocci and gram-positive diplococci. From the report of case 2, the following is quoted:

> The bacteriologic report showed gram-negative bacilli, a few short chains of streptococci, large gram-positive diplococci, a few large gram-positive bacilli and many gram-positive cocci. Cultures from the wound after forty-eight hours in a blood sugar medium showed many diphtheroid bacilli, many small gram-negative bacilli (colon bacilli), a few short chains of streptococci and many gram-positive staphylococci. Cultures in plain agar showed nonhemolytic streptococci, nonhemolytic staphylococci and Staphylococcus aureus. Cultures in dextrose broth showed many gram-positive cocci (staphylococci), a few large gram-positive diplococci, occasional short and long chain streptococci and many small and large bacilli, both gram-negative and gram-positive.

12. Alexander: Ann. Surg. **84**:461 (Sept.) 1926.

In case 3, in which there was a fulminating infection, a short chain streptococcus and some staphylococci were recovered after the first operation. Two months later the predominating organisms were found to be streptococci, diplococci and Alcaligenes bookeri, together with gram-positive cocci, staphylococci and both gram-positive and gram-negative bacilli. In the case reported by Baker and Terry,[3] cultures yielded a nonhemolytic streptococcus and hemolytic Staphylococcus albus.

Thorough bacteriologic studies of Brewer's cases were conducted by Meleney,[8] who was able to produce gangrenous ulcers in animals. He

Bacteriologic Data in Reported Cases

Cases	Strep-to-coccus	Staph-ylo-coccus	Gram — Bacillus	Gram + Bacillus	Gram + Coccus	Diplo-coccus	Diph-theroid Bacillus	Alcali-genes Bookeri	Micro-coccus Buc-calis	Micro-coccus Lique-faciens
Cullen	+	..	..	..	..	..	..	..	..	..
Christopher (S. Clin. North America **4**: 795, 1924)	..	..	+	..	−	..	..	..	..	..
Brewer and Meleney	+	+	..	..	..	..	−	..	..	..
Horsley |1	+	..	+	..	−	−	..	..	..	..
Horsley |2	+	+	−	+	+	+	−	..	..	..
Horsley |3	+	+	..	+	+	+	..	+	..	..
Alexander	+	+	..	..	..	..	..	..	+	+
Shipley (Ann. Surg. **87**: 245, 1928)	+	..	..	..	..	..	..	..	..	..
Mayeda (Deutsche Ztschr. f. Chir. **196**: 311, 1926)	..	..	..	..	..	..	+	..	..	..
Gordon (U. S. Vet. Bur. M. Bull. **4**: 1045, 1928)	+	..	..	..	+	..	+	..	..	..
Lynn	+	+	+	..	..	..	..	..	..	..
Baker and Terry	+	+	..	..	..	..	..	..	..	..
Duemling and Elston	+	+	+	..	..	..	..	..	..	..

found a nonhemolytic streptococcus, a hemolytic staphylococcus and a diphtheroid bacillus. Injection of the first two organisms together into animals caused gangrenous ulcers, whereas separate inoculations produced very little reaction. From this he deduced that there was a synergistic and symbiotic relationship between these two organisms, and that the streptococcus prepared the way for the gangrenous process, but that Staphylococcus aureus was necessary for its actual production. In this connection it is of more than passing interest to note (table), that a streptococcus was found in every case in which bacteriologic studies were made, and that the staphylococcus is the second most frequent organism found. Horsley [6] concurred in Meleney's [8] explanation of the rôle of these two organisms in the production of the gangrenous ulcers. In our case streptococci, Staphylococcus aureus and gram-negative bacilli were isolated from the lesion.

PATHOLOGY

These progressive gangrenous ulcerations usually develop about a drainage opening, or about a stitch hole, on from the seventh to the twenty-first postoperative day, occurring most frequently in septic cases, as in perforation of the appendix or drainage from the gallbladder or the intestinal tract. The condition begins as a small painful, swollen, reddish-purple lesion, which breaks down and ulcerates with a necrotic center within from forty-eight to seventy-two hours after the onset. The edges of this ulcerative area are elevated and are surrounded by a distinct area of redness, in which the pain is most severe. The center is covered with foul-smelling, necrotic, tough, stringy tissue. The lesion involves the skin, subcutaneous tissue and fascia, and extends rapidly in a serpiginous manner, gaining an inch a day in extension. If the ulcerating area is not stopped, it will involve the whole abdominal wall within a period of a few weeks. Microscopically one finds liquefaction necrosis and abscess formation.

CONCLUSIONS

1. Herein is reported a case of postoperative gangrenous ulceration of the abdominal wall following operation for a ruptured gastric ulcer.

2. From the number of cases reported and their similarity in appearance, clinical course and bacteriologic data, this condition is thought to be a definite clinical entity.

3. The etiologic factors are probably the streptococcus and the staphylococcus, which invade the tissues in symbiotic relationship.

4. Attention is called to the use of bacteriophage in successfully controlling recurrences in our case. This may have controlled the process at its very beginning.

5. Attention is also called to the use of oxyquinoline sulphate and scarlet red impregnated gauze as an epithelial stimulant and for relief from pain attendant on changing dressings.

MYCOSIS FUNGOIDES

REPORT OF A CASE WITH AUTOPSY

OLIVER S. ORMSBY, M.D.
AND
CLARK W. FINNERUD, M.D.
WITH THE COLLABORATION OF CARL APFELBACH, M.D.
CHICAGO

Mycosis fungoides was first described by Alibert in the year 1812 and has been intensively studied both clinically and histologically throughout its long history. It is still an uncommon disorder, and on account of its complicated clinical features and apparently variable histologic structure it has presented problems the solution of which has baffled most investigators. Confusion has been injected by reports of cases that terminated in leukemia.[1] Other cases are recorded in which the histologic process was interpreted by the reporter to be that of Hodgkin's disease [2] or of lymphosarcoma.[3] With improved methods of staining and newly discovered tests for distinguishing cell characteristics, both dermatologic and general pathologists have attempted to solve the problem. Much valuable information has been added by these researches, but still the problem remains unsolved. The question of its being a disease *sui generis* or merely a link in a chain of a series of diseases has been a controversial subject. Another controversial point has been whether the disease is a new growth or an inflammatory or granulomatous condition. In several instances lymphosarcoma, Hodgkin's disease or leukemia has been found in association with a mycosis fungoides symptom complex.

Several competent observers have found a characteristic histologic architecture both in the early superficial (premycotic) lesions and in the tumor-like and ulcerating lesions of the later stages. Others have failed to find such characteristic structure in any of the early lesions other than those with a general erythroderma. In a few instances, in place of the characteristic structure in the fungoid lesions, a lymphosarcoma structure has been reported and described. Notwithstanding all this apparent confusion, it must be admitted that there is a symptom complex in which diverse superficial lesions occur which are usually lichenoid.

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 3, 1932.

1. Pardee, L. C., and Zeit, F. R.: Mycosis Fungoides, J. Cutan. Dis. **29**: 7, 1911.

2. Fraser, J. F.: The Pathology of Mycosis Fungoides, J. Cutan. Dis. **35**: 793, 1917.

3. Fraser, J. F.: The Interpretation of Mycosis Fungoides as a Variety of Lympho-Sarcoma, Arch. Dermat. & Syph. **11**:425 (April) 1925.

psoriasiform or eczematous, commonly accompanied by intense itching; that these lesions may be transitory or more or less persistent; that they usually develop in circles or segments of circles; that sooner or later tumor-like fungating lesions appear which also may be transient, disappearing at times leaving no trace, and that invariably a fatal termination results. In these cases the skin is the chief area of attack while the glands and viscera are involved to a minor degree if at all.

The following case is recorded, as it gave opportunity for extended observation and study.

REPORT OF CASE

History and Course.—A woman, aged 32, was first seen on July 8, 1919, and was under continued observation and treatment until her death on July 24, 1931. When she was first seen the disease was of three years' duration. The lesions then consisted of elevated, infiltrated, lichenoid, scaling areas varying in size from that of a pea to that of a palm. These were irregular, circular or ringed or presented segments of circles; they varied in hue from dull red to normal, were situated on the arms, neck, trunk and thighs, and were intensely pruritic. The lesions began as patches which became elevated and then broke up into circles and parts of circles. The circular lesions had an elevated margin with a clear center. After several years eczematous patches occurred, and finally ulcerations having the same contour as the original lichenoid areas. As time elapsed, practically the entire cutaneous surface was attacked. For several years the number of active areas varied from eight to thirty or forty. All lesions responded readily to roentgen therapy, one unit administered in divided doses being sufficient to clear a patch. The disease was never entirely quiescent, but there were many periods of three or more months' duration when no new lesions developed and the patient was comfortable; these periods followed courses of roentgen therapy.

During the last three years some edema with weeping occurred on the legs and feet. There was never any change in the urine.

Arsenic and iron were given from the beginning, iron in large doses to combat the secondary anemia. Some arsphenamine was used. Calcium chloride and calcium gluconate gave the most relief from itching. Sodium thiosulphate improved the toxicity when much absorption occurred from the weeping surfaces. In 1929, twenty-three injections of antimony and potassium tartrate were given at the suggestion of Dr. Mook. These had no appreciable effect. Phototherapy was used over the whole cutaneous surface for a year. The tanning that resulted was of some service in relieving the itching.

Thirty-four examinations of the blood were made during the twelve years. The hemoglobin varied from 47 to 90 per cent. It was in the eighties most of the time. On the first examination it was 60 per cent. It was increased by the continuous use of iron and later by the administration of liver and other substances. The red cells varied from 3,650,000 to 4,340,000, and the leukocytes from 9,800 to 12,600. The number of the latter seemed to depend somewhat on the activity of the moist symptoms. Five differential counts are presented in the following table.

It seems probable that fungoid lesions were prevented through the ready response to roentgen therapy. This method has always been of value as a palliative, but not as a curative, measure.

Autopsy Report (Essential Observations).—Anatomic Diagnosis: The diagnosis was generalized desquamation, brown pigmentation and disseminated ulcers

of the skin (mycosis fungoides); slight hyperplasia of the cervical, axillary, periaortic, abdominal and inguinal lymph glands; hyperplasia of the spleen; marked emaciation; acute mucopurulent bronchitis; acute emphysema of the lungs; anemia, and old healed miliary tuberculosis of the kidneys, liver, spleen and lungs.

The body was that of a thin, short, white woman about 50 years old. Rigor mortis was only slightly present, and the body was warm. The skin was extensively changed by superficial desquamation and irregular brown regions. There were a few ulcers, from 1 to 2 cm. in diameter, on the inside of the left knee and on the front of the right knee, four on the fingers of the right hand and one in the scalp. These were flat, dry and irregularly oval and had slightly elevated margins. There were palpable lymph glands in the right inguinal region. There was no noteworthy change in the peritoneal or pleural cavities, except as mentioned in the anatomic diagnosis.

The spleen was about normal in size, but surfaces made by sectioning were markedly altered by gray, rounded, slightly elevated regions averaging 3 mm. in diameter, and there were several to every square centimeter. These were separated by a pale red pulp.

Differential Count

Year	Polymorphonuclear Leukocytes, per Cent	Lymphocytes, per Cent	Eosinophils, per Cent	Transitionals, per Cent
1922	68	30	2	
1923	66	28	3	3
1924	64	30	4	2
1925	72	22	2	4
1931	60	33	4	4

The lymph glands that were large averaged 1 cm. in length, and on surfaces made by sectioning they were soft and gray-pink.

Histologic Examination: Tissues were fixed in alcohol and Zenker's solution, embedded in paraffin and celloidin, and stained with hematoxylin-eosin, Weigert's elastic tissue stain, acid orcein-hematoxylin, Mallory's aniline blue, Unna's polychrome methylene blue, Pappenheim's pyronin methyl green, van Gieson's stain, Mallory's phosphotungstic acid hematoxylin, Bielschowsky's silver impregnation stain and the oxydase reaction method.

A lymph gland from the periaortic abdominal chain showed the normal architecture distinctly altered so far as the follicles were concerned. In only a few places was there any resemblance to germinal centers or follicles. In their place there was a uniform structure (fig. 1) made up of a delicate fibrillar network containing lymphocytes, eosinophilic polymorphonuclear leukocytes, a few lymph channels and a very few larger cells with a large nucleus, sparse chromatin and an abundance of eosinophilic cytoplasm. At least one fourth of the cells were reticular cells. There was very little difference between the cortex and the medulla of this gland. The diagnosis was chronic hyperplastic lymphadenitis. Nodes from the axillary and mediastinal regions were not changed in any noteworthy way.

Bone marrow from the right femur showed adipose tissue still present, but between the fat cells there was a proliferation of granulocytes and erythrocytes. Granulopoiesis was slightly more abundant than erythropoiesis, and in addition there was a preponderance of eosinophilic granulocytes.

The small bowel showed no increase in the lymphoid tissue of the submucosa.

The spleen was markedly altered. Malpighian corpuscles with collections of lymphocytes around the central artery were sparse. Surrounding arteries of the size of the central arteries there were lobular-like regions (fig. 2) about one-quarter

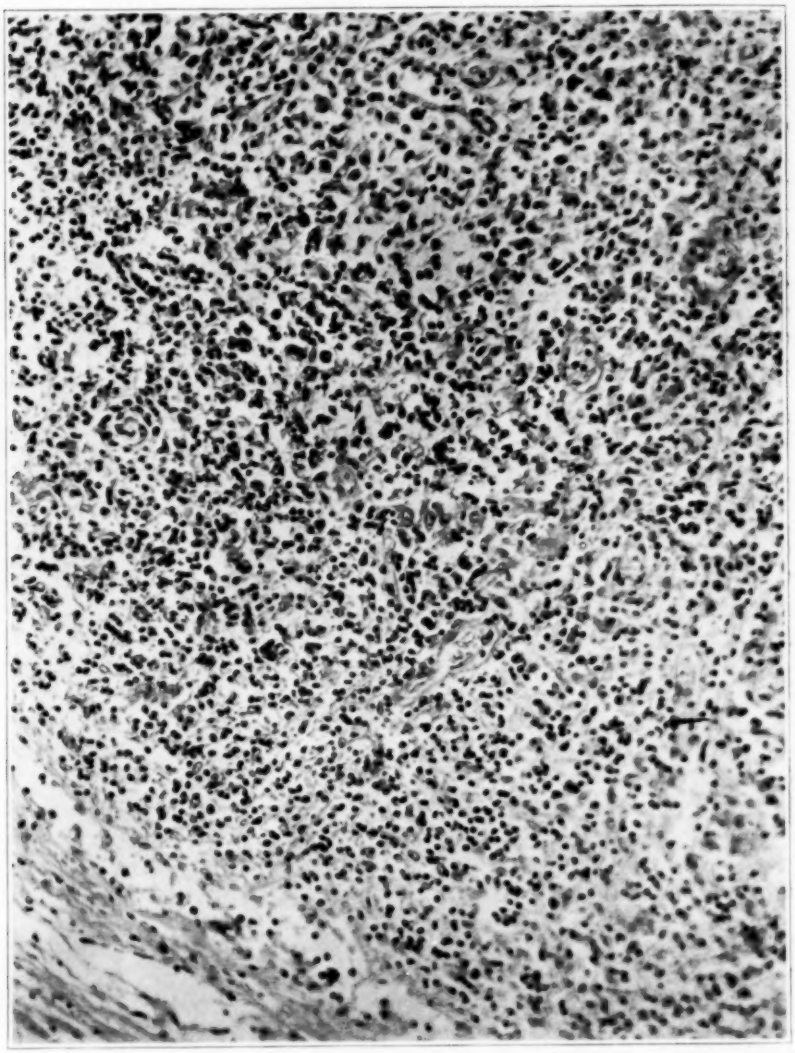

Fig. 1.—Photomicrograph (about × 360) of the cortex of an abdominal periaortic lymph gland showing replacement of follicles by a uniform tissue consisting chiefly of reticulum, lymphocytes, lymph channels and endothelial-like cells.

or one-third the size of a low power field (× 80). These were in most instances oval. They were surrounded and separated from one another by a dense stroma with venous sinuses in it. In the pseudolobule itself the cells were composed

about equally of lymphocytes and slightly larger cells with a pale nucleus and abundant cytoplasm, some of which were definitely associated with the reticulum. Polymorphonuclear eosinophilic cells were not numerous (fig. 3).

In some of the lobules the central portion was made up of reticulum, the cells and fibers of which stained poorly, resembling slightly regions of coagulation necrosis. In aniline blue preparations, however, no fibrin was demonstrable in such regions. The interpretation of the histologic changes was disseminated hyperplasia of the reticulum and phagocytic cells near the central arteries. The histologic diagnosis was disseminated chronic hyperplastic splenitis.

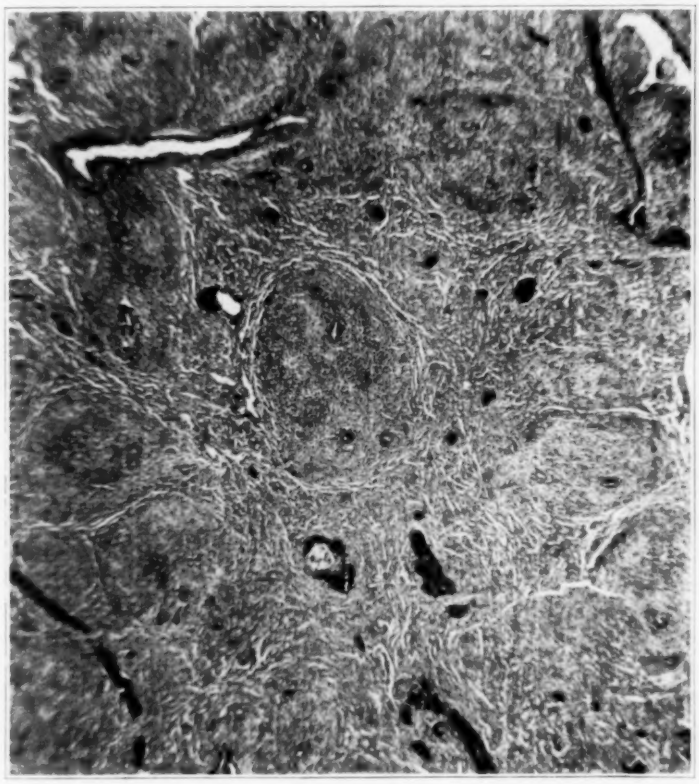

Fig. 2.—Photomicrograph (× 40) of the spleen, showing the lobule-like proliferation about the central arteries.

The histologic alterations in the spleen and periaortic abdominal lymph glands were due to inflammatory or progressive changes and not to an infiltration of neoplastic tissue. This was made clear by the fact that the original structures of the spleen were altered and not replaced. The majority of the cells, in other words, were cells that normally are present in these structures. The differences between the infiltration of the skin and the changes of the spleen and lymph glands were chiefly quantitative.

Histopathologic Changes in Cutaneous Lesions.—A specimen from a plaque on the back of the right leg removed in October, 1924, showed moderate acan-

thosis, the papillae extending in nearly all instances to within three or four layers of cells of the stratum corneum and in a few instances through the stratum granulosum to the corneum. The rete pegs dipped deeply into the corium; some of them were rounded and some clubbed or pointed. Parakeratosis was mild, but edema was marked in the lacelike reticulum of the papillary corium. There

Fig. 3.—Photomicrograph (about × 360) of the tissue about the central arteries of the spleen, showing replacement of the malpighian corpuscle by pathologic tissue resembling that in the true skin.

was an occasional miliary abscess or miliary vesicle immediately beneath the stratum corneum. Some of the epidermal cells were partially degenerated, and there was an occasional wandering cell in the epidermis. The cell infiltrate was diffuse and sharply demarcated in the papillary corium and was chiefly of the

perivascular type in the reticular corium. It consisted nearly altogether of round and connective tissue cells, the former predominating and being of the lymphocytic type. The blood vessels throughout were dilated, as were some of the lymph spaces. There was no sharp differentiation in places between the cell infiltrate and the basal layer of the epidermis (figs. 4 and 5).

Histologic sections of tissue taken at autopsy from infiltrated patches on the body showed a dense cellular infiltrate largely limited to the upper third of the corium, except for patchy deeper perivascular, perifollicular and periglandular involvement. It was situated in a delicate reticular stroma and was composed

Fig. 4.—Photomicrograph (× 60) showing acanthosis, parakeratosis, subcorneal miliary vesicle formation and distribution of infiltrate.

for the most part of basophilic cells which varied greatly in size, shape and staining characteristics, and which apparently belonged to the lymphocytic series. Eosinophils were scarce, but many cells had an eosinophilic cytoplasm. A few polymorphonuclear leukocytes were present in the lumens and in the vicinity of the well formed blood vessels of the papillary corium. This dense infiltrate had practically obliterated the rete pegs. There were moderate edema of the epidermis and papillary corium and an occasional miliary vesicle or crust (figs. 6 and 7).

Histologic sections of a nodule from the scalp removed at autopsy showed the epidermis very irregular, being thinned in places to two or three cells in depth and definitely acanthotic in others. Parakeratosis was evident in all areas

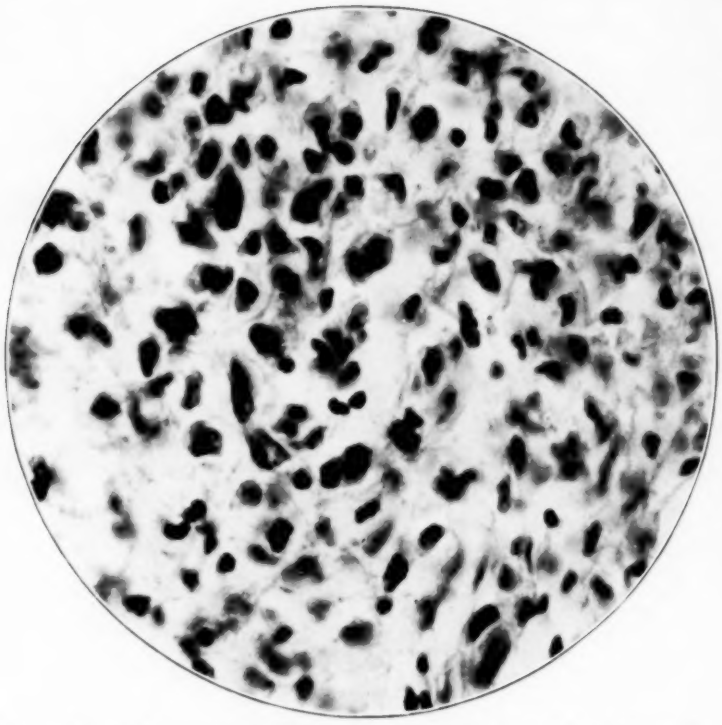

Fig. 5.—Photomicrograph (× 700) showing character of the infiltrating cells, their variation in size, shape and staining characteristics and their stroma in the form of a delicate reticulum.

Fig. 6.—Photomicrograph (× 60) of tissue taken at autopsy from a chronically infiltrated patch of the trunk, showing essentially the same changes in the corium present in figure 4, but in which the epidermis pegs and papillae have become obliterated.

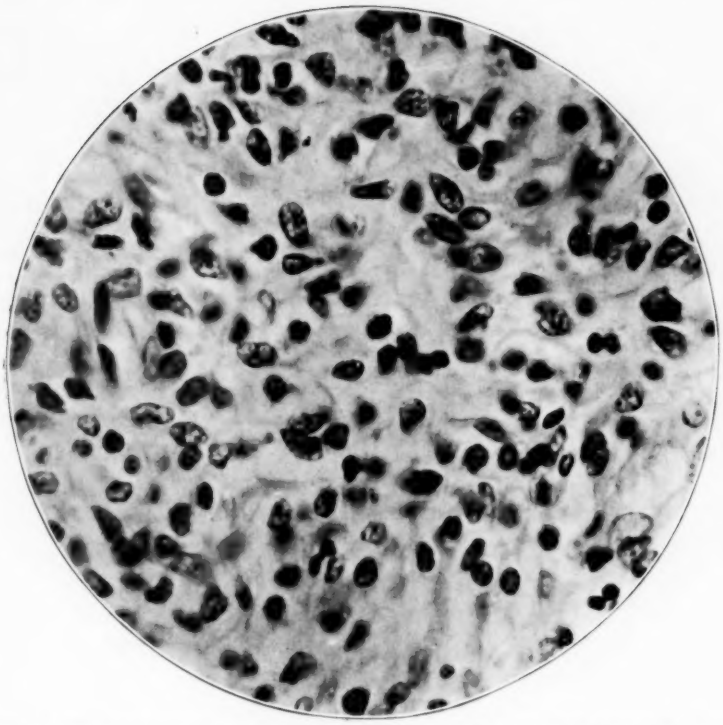

Fig. 7.—Photomicrograph (× 700) of infiltrate illustrated in figure 6, showing essentially the same cytologic changes present in the early stages of the disease.

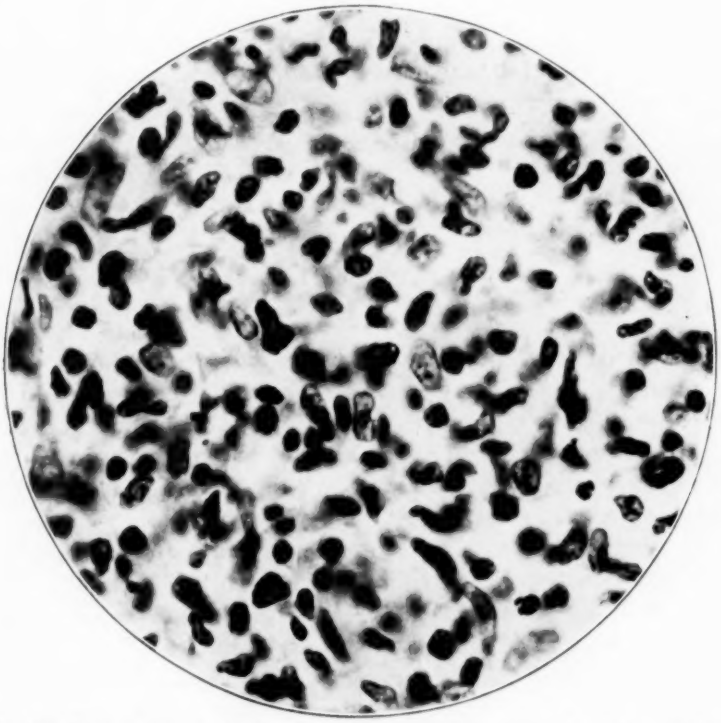

Fig. 8.—Photomicrograph (× 700) from a nodule from the scalp removed at autopsy, showing essentially the same cytologic changes present in the other cutaneous lesions, except that the chromatin content of the cells and of the stroma is more dense.

where the stratum corneum was present. Throughout the corium and extending into the hypoderm there was a dense cellular infiltration, this having replaced practically all of the normal constituents of this tissue. Capillaries were fairly numerous. In most areas the infiltrating cells were situated in a delicate reticulum, the individual cells being in close proximity to the reticular structure. The cells of this mass varied greatly in size, shape, content and staining characteristics, and for the most part they appeared to be of the lymphocytic series. The chief infiltrating cell had a round to oval nucleus, rich in chromatin, and sparse cytoplasm. Mitotic figures were present though scarce (fig. 8).

COMMENT

In this case there occurred in the skin and certain other organs a tissue reaction apparently of inflammatory nature. The changes in the spleen and probably also those in the lymph glands were similar and analogous to those in the skin, the pathologic cells in these internal structures representing a hyperplasia apparently derived from the lymphoid cells and the reticulum. Plasma cells and eosinophils, though present, were not numerous.

In the sections of the skin, aside from the psoriasiform type of proliferation of the epidermis and the associated superficial miliary vesicle and miliary abscess formation, believed by some to be characteristic changes of early mycosis fungoides, the most marked alterations were in the upper half of the cutis. There was present the polymorphous type of infiltrate, such as one sees characteristically in mycosis fungoides, the size, shape, content and staining characteristics of the cells varying greatly. Lymphoblastic, "mycotic," epithelioid and fibroblastic cells were numerous. In fewer numbers there were small mononuclear lymphocytic, large multinucleated fibroblastic, polymorphonuclear neutrophilic, eosinophilic and plasma cells. There were moderate proliferation of blood vessels, some evident mitosis and some granular cellular débris.

The changes in the true skin resembled more a reactive response of an entire system (reticular tissue of the skin) to a stimulus (toxic, infectious or other) than localized changes that characterize neoplasms. The spleen and chains of lymph glands were altered, as was the true skin, whereas other organs not related to the lymphatic system, but which are interposed between the skin and the spleen by lymph channels and blood vessels, such as the lungs, the liver and intervening chains of lymph nodes, were not altered. Also, the changes in the spleen and lymph glands were alterations of tissue normally present in these structures and obviously not a foreign tissue brought to them. We are not unmindful of the fact that the changes in the lymph glands might represent a secondary infective process from the skin.

A comparison of these observations with those commonly noted in Hodgkin's disease and in lymphosarcoma shows that in Hodgkin's dis-

ease the characteristic changes are those of a rich granulation tissue plus the usual presence of large numbers of the pathognomonic so-called Paultauf-Sternberg or Dorothy Reed cells, changes usually limited to lymph glands. Epidermal changes, if present, are not characteristic. Multinucleated large cells, when present in mycosis fungoides, though usually not closely simulating those of Hodgkin's disease, are comparatively few and are seen chiefly in early lesions, in contrast to their frequency and time of occurrence in Hodgkin's disease. The nuclear and protoplasmic detritus seen in mycosis fungoides is absent in Hodgkin's disease, the latter undergoing regression by caseation and necrosis.

In lymphosarcoma, as in sarcoma of other nature, there exists a greater uniformity of cell type. It is said that in this condition the epidermal changes are not inflammatory and that there exists a band of normal cutis between the proliferating cells and the epidermis.

The case herein reported was a typical one of mycosis fungoides presenting lesions in the prefungoid stage. Sections of the skin taken seven years before death showed a histologic structure almost identical with that in those taken at autopsy. It seems probable that fungoid lesions were held in abeyance through roentgen and other therapy.

Since 1903, roentgen irradiation has been employed as a successful palliative measure. The patient in the sixth recorded case [4] was treated by one of us over a long period with unusually good temporary results.

Our office records, which include forty cases, indicate that the chief symptoms of mycosis fungoides are exhibited in the skin. Only a few cases of Hodgkin's disease have been seen, and these, with two exceptions, showed nonspecific cutaneous lesions. The problem is one of internal medicine, as the involvement of the skin is a minor matter. Lymphosarcoma is more properly a surgical disease. Only one case appears in our private records, and that occurred as a complication in a case of poikiloderma atrophicans vasculare.

For some unexplained reason similar symptoms occur in a minor degree in different diseases, causing confusion in their differentiation. This is true of mycosis fungoides, Hodgkin's disease and lymphosarcoma. In all, however, there are predominating symptoms which make possible the distinction in most cases. In mycosis fungoides the predominating symptoms are in the skin, the minor lesions elsewhere. In Hodgkin's disease the predominating lesions are in the lymphatic glands, the minor lesions in the skin. In lymphosarcoma the predominating lesions are in localized lymphoid tissue and in mucous membranes, the skin lesions being unimportant.

The histologic observations, like the clinical manifestations, should be appraised by the predominating features. In mycosis fungoides a

4. Medicine **9**:904 (Dec.) 1903.

mixed cell infiltration is the predominating picture with, in some cases, a minor number of cells of lymphosarcoma type. In Hodgkin's disease there is also a mixed cell infiltration, but with characteristic giant cells. In lymphosarcoma the predominating picture is a uniform cellular growth with, in some cases, a minor number of the mixed cells of the other two diseases.

It is, therefore, possible, by recognizing the predominating picture, both clinical and histologic, to classify most cases properly.

The assertion that mycosis fungoides does not exist as a clinical or pathologic entity [5] does not clarify the situation particularly. We believe that the preponderance of evidence is opposed to this view.

Mycosis fungoides, Hodgkin's disease, lymphosarcoma and several other diseases united by Keim [6] under a single title appear to be closely related genetically and could well be grouped into a class of lymphoblastic diseases.

CONCLUSIONS

The case herein described presented the usual clinical picture that is characteristic of the prefungoid stage of mycosis fungoides.

The histologic picture of the cutaneous and other lesions was also characteristic of the commonly accepted conception of this disease and was interpreted as being inflammatory rather than neoplastic.

Having in mind the fact brought out by competent investigators, that certain cases would from a histologic point of view throw doubt on the existence of mycosis fungoides as an entity, we believe that the preponderance of evidence, both clinical and histologic, demands the continued recognition of this condition as a disease *sui generis*.

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5. Symmers, Douglas: Mycosis Fungoides as a Clinical and Pathologic Nonexistent, Arch. Dermat. & Syph. **25**:1 (Jan.) 1932.

6. Keim, H. L.: The Lymphoblastomas: Their Interrelationships, Arch. Dermat. & Syph. **19**:533 (April) 1929.

LYMPHOBLASTOMA (MYCOSIS FUNGOIDES) AND HEMORRHAGIC SARCOMA OF KAPOSI IN THE SAME PERSON

C. GUY LANE, M.D.
AND
ARTHUR M. GREENWOOD, M.D.
BOSTON

The uncertainty surrounding the background of both mycosis fungoides and Kaposi's sarcoma lends an added interest to the coincidental occurrence of the clinical manifestations of the two diseases in the same person. Mycosis fungoides developed first in a patient who came under our observation, and later a blood picture characteristic of a mild lymphatic leukemia appeared. In the last four months of his life a mass of nodules developed on the right foot with a few lesions elsewhere, having the histologic characteristics of Kaposi's sarcoma. Many authorities have grouped mycosis fungoides, the leukemias, Hodgkin's disease and lymphomas under the general term lymphoblastoma. This lymphoblastoma group as a whole has many puzzling features, and every unusual case in this group, while it may complicate the picture at present, may contribute with the summation of evidence to the clarification of the relationships within the group.

REPORT OF A CASE

First Admission.—F. C., aged 42, Italian, a laborer, was seen on Jan. 7, 1930. In 1928, a vague general itching appeared, without any eruption and without any other disturbance in health. The patient stated that the itching became more severe in 1929, and that indefinite thickenings appeared over the skin of the lower portion of both legs. For the past year he had had considerable perspiration after the attacks of itching. The itching had become progressively worse, and he had increasing difficulty in sleeping and working. He had been unable to work for the past few months. He had lost 15 pounds (6.8 Kg.).

In general the skin over the body was pigmented, smooth and rather dry. In numerous places there were areas of more marked pigmentation, with a purplish periphery, accompanied by slight thickening, with some scaling in most of these areas. The extremities were moist, and the skin was considerably thickened, especially over the lower portion of the legs. There were numerous small and large infiltrated plaques over the lower extremities and the hands, but these were freely movable and not adherent to underlying tissue. These plaques were covered in many places with scales, but there was no ulceration or suggestion of central softening. The rest of the physical examination gave essentially negative results.

Examination of the blood on the patient's entrance to the hospital showed: red cells, 4,870,000; hemoglobin, 65 per cent, and white cells, 21,400. A differ-

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ential count revealed: polymorphonuclears, 57; lymphocytes, 30; large mononuclears, 6, and eosinophils, 7. There was only slight achromia, and the platelets were normal. The Wassermann and Hinton tests were negative; the nonprotein nitrogen was 46, and the blood calcium, 8.9. On examination the urine was normal.

Biopsy of a gland in the neck showed a picture consistent with lymphoblastoma. The skin picture was characteristic of mycosis fungoides, and biopsy of the lymph node confirmed this diagnosis.

On this admission, high voltage roentgen therapy, with a filter of 0.5 mm. of copper and 4 mm. of celluloid and two thirds of an erythema dose, was administered to both groins and each axilla, and a small amount of superficial irradiation was given to the skin of the body and legs. The patient was discharged on Jan. 22, 1930.

Second Admission.—On the patient's second admission to the hospital, on March 4, the condition was worse, and it had been necessary for him to remain in bed most of the time while he was at home. It had been almost impossible for him to sleep on account of the itching.

Examination made at this time revealed that the skin was very dry, especially over the extremities, where there was marked thickening. In this thickened skin, especially over the extremities and chest, there were innumerable hard papules, varying in size from that of a pinhead to that of a large split pea. There were also a few papules on the scalp and face. Many of them were excoriated, crusted and oozing. These nodules were not tender; they were somewhat red and freely movable. They were far more numerous over the feet, ankles, legs and thighs. The distribution was about equal over the flexor and the extensor surfaces. The palms, soles and trunk, except the upper part of the chest, were free from these nodules. Below the umbilicus there was an area about 6 cm. in diameter where there were a number of sharply outlined, rather round areas, devoid of pigment. About the genitals and in both axillae were blotchy areas where white skin alternated with sharply outlined pigmented areas. The legs and ankles were swollen, and there was considerable pitting on pressure. The nails were dry, atrophic and rough. There was the same marked enlargement of all the cervical, axillary and inguinal glands, and some of the glands in both groins were as large as walnuts. The glands were moderately hard and not tender. The liver and spleen were not felt.

On this admission examination of the blood showed: red cells, 4,470,000; hemoglobin, 70 per cent, and white cells, 14,100, with polymorphonuclears, 38; lymphocytes, 56; large mononuclears, 3; eosinophils, 5, and basophils, 1. There were no abnormal cells and no achromia or poikilocytosis. The platelets were normal.

On this admission neoarsphenamine was given in conjunction with high voltage roentgen therapy, two thirds of an erythema dose being used with the same filtration as before, to each groin and to the spleen. There was no definite change in the condition when the patient was discharged on March 17.

Third Admission.—On April 28, the patient was admitted to the hospital for the third time. He had remained in bed while at home, and his condition on admission was unimproved. At this time thorough irradiation with high voltage roentgen therapy, with the same dosage as before, was given to glandular areas, including each side of the neck, each groin and each axilla. The patient also received an injection of neoarsphenamine during his stay in the hospital. On discharge, on May 14, the general condition seemed a bit better, although there was no marked change in the condition of the skin.

Fourth Admission.—The patient was not admitted to the hospital again until Feb. 24, 1931. In the interval, the itching had been severe and constant, and he was

badly excoriated. During the last few weeks before admission he had had a particularly difficult time, not only with the itching, but with marked swelling of both feet and legs, with numerous fissures on the hands, more redness and thickening of the skin and an increase in the size of the nodules, especially those on the lower right portion of the leg. The skin was generally red and thickened, with considerable pigmentation, generally distributed, and some patchy localization. There was marked tense swelling of the lower part of both legs, especially the right one, which was definitely larger than the left. Over the outer side of the right ankle, particularly, there was a marked verrucous appearance (fig. 1), with considerable infiltration, pigmentation and excoriated nodules extending high up on the leg. The feet and hands were badly fissured, with numerous cracks and oozing. There were numerous nodules, similar to the ones which have been described. The spleen was palpable 3 cm. below the costal margin. The glands were still markedly enlarged.

Fig. 1.—Lateral view of the right leg taken on Feb. 26, 1931. Note the verrucous appearance about the ankles.

Changes in the Condition of the Blood as Shown by Cell Counts

Date	White Cells	Polymorphonuclears	Lymphocytes	Monocytes	Eosinophils	Basophils	Comment
2/24	32,800	30	66	3	0	0	Few myeloblasts
3/ 1	67,200	40	58	2	0	0	Few lymphoblasts
3/ 2	38,500	35	63	2	1	0	Large lymphocytes
3/ 5	40,500	..	..	..	..	..	Mostly lymphocytes
3/15	27,700	53	47	0	0	0	Mostly large lymphocytes
3/23	30,000	6	94	0	0	0	Small and medium lymphocytes
4/13	23,000	14	86	0	0	0	Mostly small lymphocytes
5/ 4	26,200	24	76	0	0	0	Small and medium lymphocytes

On the patient's fourth admission the blood count showed: red cells, 4,400,000; hemoglobin, 80 per cent, and white corpuscles, 32,800.

The change in the condition of the blood during this admission is shown by the accompanying table.

During this admission there was a definite increase in the signs of mycosis fungoides, and in addition numerous infections developed, including an abscess on the back of the hand and a carbuncle on the neck, with several other infected areas. These occurred mostly in the first part of the patient's stay and gradually quieted down. Later there occurred a change in the blood picture, with a white cell count rising as high as 67,200, and the percentage of lympocytes as high as 94.

Observations made at biopsy of a section taken from the sole of his right foot, although not diagnostic of a lymphoblastoma involving the skin, were consistent with it.

Roentgenograms of the chest and the long bones were negative. Three cultures of the blood showed no growth. A culture of the pus from a leg showed a hemolytic streptococcus and Staphylococcus aureus.

At this time, high voltage radiation was administered over the spleen, one half of an erythema dose being given posteriorly and one fourth anteriorly. For the

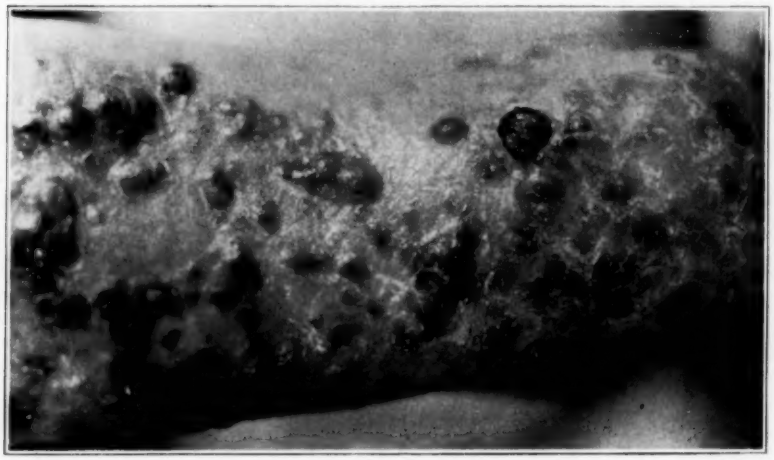

Fig. 2.—The right sole on May 14, 1931. Compare with the appearance in figure 4. Note the pigment in the tumors.

soles of the feet, where the new type of tumors had appeared, one fourth of an erythema dose was used. In addition, superficial unfiltered radiation was administered generally over the body at intervals during his stay.

During this period, new lesions appeared on the sole of the right foot, which were not typical of mycosis fungoides but had rather the appearance of Kaposi's sarcoma. This different type of nodule developed on the right foot first. The nodules became increasingly numerous while the patient was in the hospital; they were round, dome-shaped, rather smooth and shiny, somewhat pigmented and red, rising abruptly from the skin. They appeared with great frequency on the right sole particularly (fig. 2), and gradually extended up to the ankle and leg. They were entirely different from the flatter, browner, more diffuse, thickened plaques and tumors which had previously appeared as a part of the mycosis fungoides. The new tumors had progressed rapidly after the patient's discharge from the hospital on May 22, but the general condition of the skin seemed better. The fissures in his hands were definitely better, and there was a little less itching.

Biopsy of one of these new nodules showed a picture characteristic of hemorrhagic sarcoma of Kaposi.

Fig. 3.—Inner side of right leg on July 7, 1931. Compare with the appearance in figure 1 five months earlier.

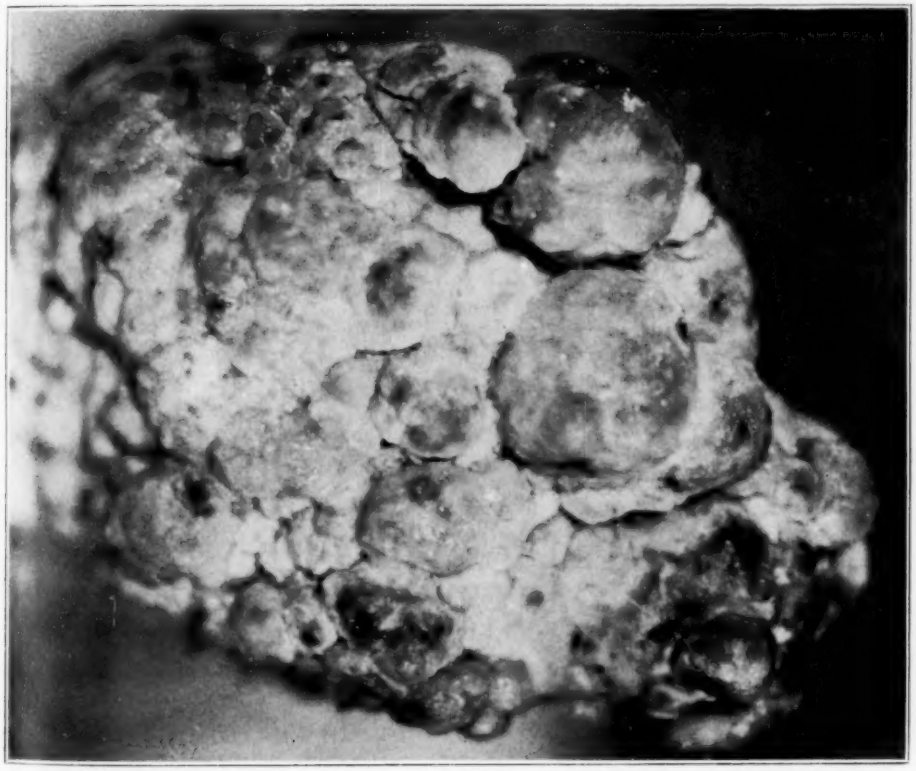

Fig. 4.—Anterior aspect of the right sole on July 7, 1931. Compare with figure 2 taken three months earlier.

Fifth Admission.—The patient was admitted for the fifth and last time on July 6. It had been necessary for him to remain in bed, and the condition had become gradually worse. The tumors on the right foot had increased so markedly that it was difficult to distinguish the toes from the tumors (fig. 4).

The tumors had extended up the right leg and had appeared on the left foot. Figure 3 shows the condition of the right leg. There was considerable discharge with a very foul odor. The leg was extremely painful. The itching had been very severe, but was somewhat submerged by the constant pain in the right leg. There were the same general dryness, scaling and thickening of the skin which had been present before, and the glands were similarly enlarged. There was considerable fissuring on both hands and feet. The preauricular and epitrochlear glands had become enlarged.

The blood showed: red cells, 2,650,000; hemoglobin, 55 per cent, and white corpuscles, 19,600, with polymorphonuclears, 24; lymphocytes, 72; transitionals, 2; eosinophils, 2, and basophils, 0. There were many large mononuclear cells, premature lymphocytes, some achromia and slight anisocytosis.

A Gritti-Stokes amputation was finally performed on July 16, with the patient under avertin and ether anesthesia.

The pathologic report on the amputated leg agreed with the previous diagnosis of Kaposi's sarcoma and mycosis fungoides.[1]

Autopsy.—The patient died on July 18, and an autopsy was performed by Dr. Tracy B. Mallory on the same day.

The anatomic diagnosis was as follows: multiple hemorrhagic sarcoma of Kaposi, mycosis fungoides, operative wound from the amputation of the right leg, septicemia, Streptococcus viridans, bronchopneumonia, partial atelectasis, cholelithiasis and diverticula of the jejunum.

The clinical diagnosis post mortem was mycosis fungoides and lymphosarcoma.

The skin appeared dry and scaly, particularly so over the head and neck. There was exfoliation in scales from 1 to 3 mm. in diameter. In addition, the skin was covered with bluish-purple, nonelevated patches, measuring up to approximately 4 mm. in diameter. These were most marked over the upper part of the thorax, neck and back. The skin felt thickened and seemed fixed to the subcutaneous tissues. There was also a slight but definite edema over the remaining portion of the body. The scrotum and the lips showed marked edema. Over the sacral region there was an ulcer 2 by 2 cm., covered with dirty necrotic tissue, from which pus and clear fluid were exuding. There was a slightly elevated, bluish-purple nodule, measuring about 1 cm. in diameter, on the skin of the medial aspect of the plantar portion of the left foot. A similar lesion of about the same size was also present in the palm of the left hand. Both nodules seemed to lie in the skin and were not fixed to the subcutaneous tissue. There was a moderate amount of subcutaneous fat, which showed definite evidence of fluid in the tissues. The muscles seemed normal. The glands on both sides of the neck were palpable, but their exact size was difficult to determine because of the stiffness of the overlying skin and tissues. The axillary and inguinal glands could be felt. There were numerous pea-sized mesenteric glands and several retroperitoneal glands ranging up to 2.5 cm. in diameter, most marked along the iliac vessels.

Microscopic examination of the lymph nodes showed: 1. The architecture was preserved. The lymphoid tissue was scanty; the cells were well differentiated. Numerous plasma cells were present. 2. The sinusoids contained numerous large

1. The Pathological Department of the Massachusetts General Hospital supplied the biopsy reports.

mononuclears and polymorphonuclears. 3. The markings were obliterated in a portion of the section, but the cells were well differentiated throughout.

The various sections of the skin, both those removed during life and those obtained post mortem, could be classified in two separate groups; one showed lesions typical of mycosis fungoides, the other, lesions typical of Kaposi's sarcoma. No transitions between the two types were found, though occasionally both lesions were present in one microscopic field (fig. 5). The mycotic lesions showed dense infiltration of the corium with mature and immature lymphocytes, with occasional eosinophils. Scattered throughout were multinucleated cells suggesting tumor giant

Fig. 5.—Photomicrograph (low power) of a section from amputated leg, showing masses of spindle cells and infiltration of lymphocytes, some of which are immature. A diagnosis of Kaposi's sarcoma and mycosis fungoides was made.

cells; their nuclei ranged in shape from oval to spindle, the cytoplasm was spindle-shaped or stellate, and the appearance suggested a fibroblastic rather than a lymphocytic origin. Mitotic figures were present in small numbers. No multiple mitoses were seen. The areas showing the Kaposi tumor were found on both legs. They showed a rapidly growing, infiltrating tumor consisting for the most part of spindle-shaped cells and large thin-walled capillaries. Many spaces filled with red blood cells appeared to be bounded only by the spindle cells. In some of the sections retrogressive areas showing dense collagen formation and a considerable deposit of hemosiderin were found. In one section taken from the fourth biopsy a phosphotungstic acid stain appeared to show fibrils on some of the tumor cells.

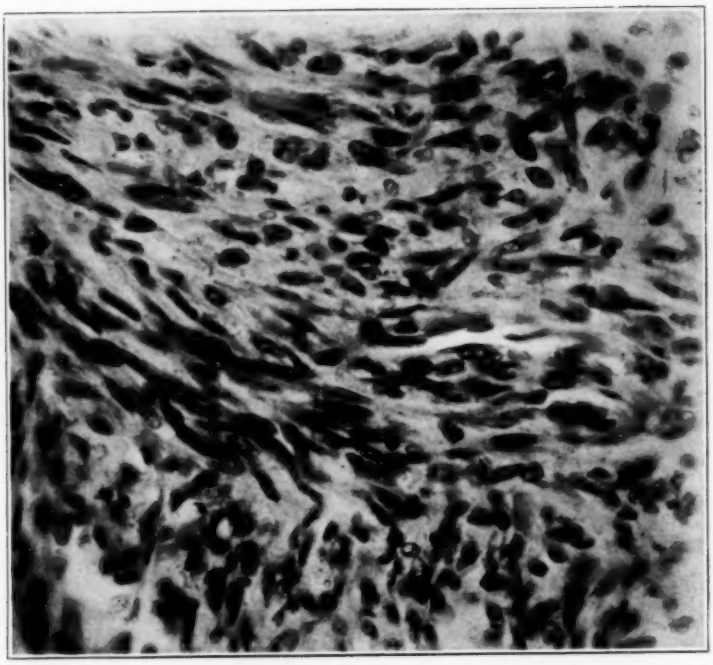

Fig. 6.—Photomicrograph (× 600) of a section of Kaposi's sarcoma. This is high power magnification of part of area shown at left in figure 5.

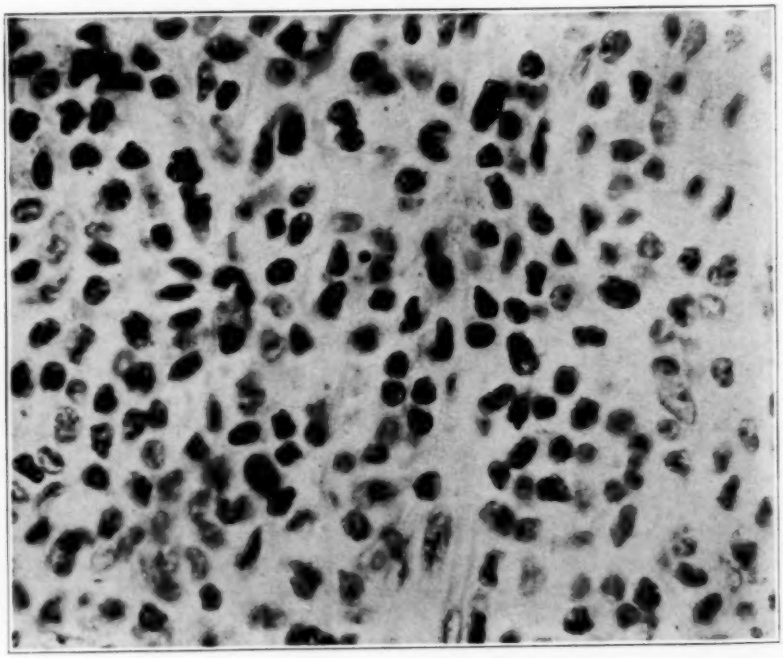

Fig. 7.—Photomicrograph (× 800) of the infiltrate of abnormal lymphocytes shown beneath the epithelium at the right of the section shown in figure 5.

COMMENT

In commenting on this case we believe it can be discussed most logically from its three main aspects, that of mycosis fungoides, that of leukemia and that of Kaposi's sarcoma.

From the beginning this case presented the classic signs of the clinical entity which is known as mycosis fungoides. All will agree that in the minds of dermatologists such objective appearances constitute a definite entity. But into this definite clinical picture certain puzzling feature are injected at times. Fraser [2] and others have reported cases in which there was lymphatic leukemia, and visceral and muscular involvement, with a histologic appearance of lymphosarcoma. Other observations of a similar nature have been reported. Symmers [3] recently stated that the tumors in the skin in cases called mycosis fungoides are attended by histologic changes of three distinct types: (1) that of Hodgkin's disease, (2) that of a reticulum cell sarcoma and (3) that of a lymphosarcoma. When one finds these clinical manifestations associated at some time during their course with blood pictures which all agree are those of a lymphatic leukemia or with enlarged lymph nodes which cannot be distinguished histologically from lymphoblastoma, perhaps with lesions in other organs which are lymphoblastomatous, and when the lesions in the skin which give the distinguishing features are not to be differentiated in many instances from other forms of lymphoblastoma, it seems logical to class mycosis fungoides as a variety of a larger group of malignant conditions of the blood, the lymphoblastomas. The term mycosis fungoides should, however, be preserved.

This case also showed an increased white count and a considerable excess of lymphocytes. The highest count occurred just before the marked infections developed, and as the infection improved the percentage of lymphocytes climbed to their highest level. The evidence is sufficient, we believe, to indicate a mild type of lymphatic leukemia. It is our opinion that numerous cases of mycosis fungoides will show abnormal changes in the blood at some time during their course. To support this view, we have reviewed briefly the seventeen cases at the Massachusetts General Hospital in the last ten years in which a diagnosis of mycosis fungoides has been made. There were four with abnormal blood pictures, or 23.4 per cent of the group. Clinically the condition was mycosis fungoides, but the abnormal cells of the blood picture varied widely.

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2. Fraser, J. Frank: Mycosis Fungoides: Its Relation to Leukemia and Lymphosarcoma, Arch. Dermat. & Syph. **12**:814 (Dec.) 1925.

3. Symmers, Douglas: Mycosis Fungoides as a Clinical and Pathologic Nonexistent, Arch. Dermat. & Syph. **25**:1 (Jan.) 1932.

The occurrence of lymphatic leukemia and Kaposi's sarcoma is unusual. Cole and Crump,[4] in 1920, reported the only case found, a case in which the white cell count rose to 200,000 and the percentage of lymphocytes to 90.

In this picture of a lymphoblastoma of the mycosis fungoides type there appeared late in the disease a different kind of tumor consistent clinically with Kaposi's sarcoma, the diagnosis of which was confirmed microscopically. It is true that this sarcoma usually has a much more chronic course, and that the pigmentation is usually a more marked feature of the disease, but the diagnosis was confirmed by several pathologists after a study of the sections.

The many different histologic interpretations of this tumor have been well summarized in the reports of Dillard and Weidman [5] and Pautrier and Diss.[6] The most recent interpretation has been offered by the two latter authors in following the special staining methods of Masson.[7] They conclude that the condition called Kaposi's sarcoma is not a sarcoma or a purely inflammatory lesion, but they see it as a dysgenesis of the vessels and their neuromuscular annexes on one side, and of their schwannian elements on the other side. Still later Hudelo and Cailliau [8] by similar methods tend to confirm this view, and point out that the pseudosarcomatosis of Kaposi presents striking analogies to von Recklinghausen's disease. They feel that the nerve elements in the vessel walls irritated by the circulating toxins may set up the tumor process in the vessels and connective tissue which eventuates in the Kaposi tumor. Pautrier and Diss [6] expressed the belief that the Wagner-Meissner bodies (glomi) are the starting point of this process. Hudelo and Cailliau,[8] however, pointed out that no traces, or insufficient traces, of these bodies were found to bring this about, and stated the opinion that the normal nerve elements in the vessel walls may be capable of originating the tumor. It is only fair to say that some of the most

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4. Cole, Harold N., and Crump, Edward S.: Report of Two Cases of Idiopathic Hemorrhagic Sarcoma (Kaposi), the First Complicated with Lymphatic Leukemia, Arch. Dermat. & Syph. **38**:283 (March) 1920.

5. Dillard, G. J., and Weidman, F. D.: Multiple Hemorrhagic Sarcoma of Kaposi, Arch. Dermat. & Syph. **11**:203 (Feb.) 1925.

6. Pautrier, L. M., and Diss, A.: Kaposi's Idiopathic Sarcoma Is Not a Genuine Sarcoma but a Neurovascular Dysgenesis, Brit. J. Dermat. **41**:93 (March) 1929.

7. Masson, P.: Mémoires Originaux: Les naevi pigmentaires tumeurs nerveuses, Ann. d'anat. path. **3**:417 (May); 657 (July) 1926.

8. Hudelo, L., and Cailliau, F.: La sarcomatose idiopathique pigmentaire multiple de Kaposi et ses interprétations histogénétiques et pathogéniques, Ann. de dermat. et syph. **2**:417 (April) 1931.

competent pathologists in this country, while agreeing with Masson's original work on melanomas, do not consider Pautrier's or Hudelo's cases as proved.

Another point of view on the subject is that of Ewing,[9] who stated that the sarcoma of Kaposi is capable of developing genuine characteristics of a malignant tumor, and that the final tumor is a spindle cell sarcoma.

Perhaps the most interesting point raised by the case reported in this article concerns the relationship of this tumor to the lymphoblastomatous process. Is this occurrence a mere coincidence, or is there a causal factor of common or related origin? If it is more than coincidence more cases would have appeared and been reported, though out of his pathologic experience Warthin [10] stated that it is possible that some of the conditions diagnosed clinically as multiple hemorrhagic sarcoma of Kaposi may be related to mycosis fungoides. In a personal communication, Wolbach agreed that these two processes may have some common relation, because the cells involved are all of mesoblastic origin. The marked involvement of the right leg from the start of the original process and the extreme rapidity of growth of the newer tumor suggest at least that the lymphoblastomatous background favored the development and course of the Kaposi nodules. These processes are probably coincidental, but it is an interesting supposition, without stretching too much the bounds of probability, to imagine that the same circulating irritant might in a single case set up a tumor process which would manifest itself, as in this instance, as a lymphoblastoma on the one hand, and as a Kaposi sarcoma on the other, the cells in both processes being of the same mesenchymal origin.

SUMMARY

A case with autopsy observations is reported in which mycosis fungoides, lymphatic leukemia and Kaposi's sarcoma occurred in the same person.

We believe that mycosis fungoides should be classed as a variety of a much larger group, that of lymphoblastoma.

A review of seventeen cases of mycosis fungoides at the Massachusetts General Hospital in the last few years reveals that 23.4 per cent of the patients showed an abnormal blood picture.

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9. Ewing, James: Neoplastic Diseases, Philadelphia, ed. 3, W. B. Saunders Company, 1928, p. 270.

10. Warthin, A. S.: Genetic Neoplastic Relationships of Hodgkin's Disease, Aleukemic and Leukemic Lymphoblastoma and Mycosis Fungoides, Ann. Surg. **93**:153 (Jan.) 1931.

Attention is called to the newer suggestions concerning the interpretation of the histologic features of Kaposi's sarcoma—its derivation from nerve sheath and vascular cells.

No conclusion can be drawn as yet regarding the relationship of mycosis fungoides and Kaposi's sarcoma, although the possibility of a common exciting agent or factor is suggested.

DISCUSSION ON PAPERS OF DRS. ORMSBY, FINNERUD AND APFELBACH AND DRS. LANE AND GREENWOOD

Dr. Udo J. Wile, Ann Arbor, Mich.: Dr. Ormsby's case is interesting because of the uniformity of findings seen so early in the course of the disease and the fact that the results of necropsy confirmed the manifestations that were present when the patient was first observed. I think that while this is not unique it is not the rule.

I think that the opinions that Dr. Ormsby and Dr. Lane have expressed can be reconciled. Certainly there is a good deal of evidence to show that some of the tumors are definitely neoplastic rather than inflammatory. I think that the point Dr. Ormsby made about granuloma fungoides being an entity is well taken, for one can easily make a diagnosis clinically. I think, however, that microscopically mycosis fungoides can vary from the picture of lymphosarcomatosus infiltration to the type that Dr. Omsby observed in his case. I have one case on record in which there could be no doubt of the clinical diagnosis, and in which the tumors were a solid mass of eosinophilic cells and remained so until death.

It was interesting to hear that 22 per cent of Dr. Lane's cases showed an unusual white blood cell count. It has been stated that the majority of cases of mycosis fungoides do not show changes in the blood and spleen of the same type found in the tumors. I am convinced that failure to demonstrate this is due to the fact that the majority of the patients receive roentgenotherapy, and that will bring down a lymphocyte count from 20,000 or 30,000 to below 2,000 at times. I think that if roentgenotherapy were not used many of the patients would show dyscrasias in the blood stream itself.

An attempt to bring these diseases together should not be regarded as an attempt to identify them as the same condition. They are not. They are sometimes seen together, or one clinical entity may evolve during a period of months into another. These allied conditions are perhaps related from the standpoint of the cell type or from that of fundamental cellular pathology, but I think it is a mistake because they can be grouped under the name of lymphoblastoma to say that they are all alike. There are various types, but I think there is a continued tendency to regard them as a group of diseases producing more or less similar cellular changes in the skin.

Dr. Walter J. Highman, New York: As indicated by Dr. Wile, the subject can be regarded from different points of view: from the standpoint of descriptive pathology, which makes the group of conditions fall into several distinct entities; from the general clinical standpoint, the major findings of which are in groups descriptively similar and which will point where to seek the cause and, finally, from the standpoint of pathology, in the broadest sense, which raises the still confused issue of which members of this group one is considering in terms of cytology. I think that the principles of cytology will be the final arbiter when more is known about the cells that compose the tumors.

I think, to be no vaguer about the matter than Dr. Ormsby was, that Dr. Wile's remarks in regard to the disease being an entity are going a little

too far. The striking thing, as brought out in Dr. Lane's paper, is that three separate groups of phenomena were present in one case: the tumor of the tibia, classified as mycosis, the growth classified as tumor of Kaposi and, superimposed on the whole, a leukemic blood picture. It is going too far to say that such a concatenation of symptoms is one entity. All are associated with the reticulated endothelial system, or, if one wishes, with embryonal cells.

It seems to me that the condition in Dr. Lane's case is not far removed from that in a similar case reported by Gilchrist and Ketron. The patient was suffering from Kaposi's sarcoma and died of lymphoblastomatous metastases. The authors go no further, and without any idea of being arbitrary in my conceptions of the question, it seems to me that Dr. Lane's tentative suggestion that these cases be grouped as instances of a biologic entity and that that conception be classified without some clinical cue word, such as mycosis fungoides, is at least for the present a sufficiently restrained point of view to be acceptable to any one, and a broad enough point of view to permit of future modification. Intellectually and emotionally I am entirely in sympathy with that point of view.

Dr. Hamilton Montgomery, Rochester, Minn.: I was much interested in both of these papers. I was interested in Dr. Ormsby's because in preparing my own paper I reviewed about ninety-five reports of cases of lymphoblastoma, including twenty-five cases in which the condition could be classified as mycosis fungoides and in which I studied the various laboratory and clinical findings as well as the subsequent course of the disease. I feel that mycosis fungoides should be classified with the lymphoblastomas, recognizing that in some instances a condition starting as mycosis fungoides may eventuate as one of the other types of lymphoblastoma. I do not feel that cases in which the clinical diagnosis is mycosis d'emblée are always instances of mycosis fungoides. Thus, there seems to be little justification for regarding ulcerating tumors frequently limited to one extremity as a manifestation of mycosis fungoides. It is necessary in these cases to employ the entire diagnostic armamentarium to arrive at a diagnosis. In some of the cases (Oliver's cases) the condition has proved to be mycosis fungoides; in others, such as Kren's cases and the second case reported by Dr. Goeckerman and me, it proved to be Hodgkin's disease, and still other discrete ulcerating lesions have proved to be leukemic or lymphosarcomatous infiltrations of the skin. I believe that mycosis fungoides represents a primary lymphoblastoma of the skin which, in the majority of cases, remains such and usually is limited to the skin without involvement of the glands or internal organs. The histopathologic changes in the late eczematoid and early infiltrative stages of the disease are characteristic. I cannot agree, therefore, with Symmers regarding the abandonment of this term. The other type of lymphoblastoma may also arise primarily in the skin, but this occurs rarely; usually when involvement of the skin is present it is secondary to changes in the internal organs and the hematopoietic system. Until more is known about the etiology, I believe that one should continue to try to distinguish between the various conditions included under the term lymphoblastoma.

In regard to Dr. Lane's paper, Dr. Julius Doerffel, of the University of Königsberg, has recently done some work at the Mayo Clinic on Kaposi's sarcoma and has collected about sixteen cases of the disease. He studied the disease in its various stages, and concluded that Kaposi's sarcoma starts with involvement of the reticulo-endothelial system of the skin, frequently with increase of monocytes of the blood, but that eventually it may develop into a true malignant growth. In the early stages of the disease there are small collections which

look like lymphocytes, but which under higher magnification can be recognized as lymphocytoid cells of Marchand; also there are numerous vessel wall cells. In the later stages of the disease the microscopic picture may be indistinguishable from that of sarcoma. The most distinguishing histologic feature between mycosis fungoides and Kaposi's sarcoma is the marked deposits of hemosiderin in the latter disease.

In Dr. Lane's case there can be no question either clinically or histologically but that lesions of both diseases are present. The relationship of Kaposi's sarcoma to the reticulo-endothelial system immediately calls to mind the same relationship emphasized by Fraser in regard to mycosis fungoides. Dr. Lane and Dr. Greenwood's case would seem to offer additional support for this view and also for Fraser's view regarding reticulum cell sarcoma. This subject is worthy of further detailed studies.

Dr. Oliver S. Ormsby, Chicago: I am much interested to find that every one who has discussed these papers agrees in the main with both of them. Dr. Wile's experience has been extensive, and he has established this group of lymphoblastomas. His work has been of scientific value in the study of obscure cases. Everything that he said agrees with the statements in our paper. In our case, as noted in the conclusions, the process was inflammatory.

Our chief desire was to emphasize the fact that from our standpoint one has to recognize mycosis fungoides as an entity. We stated that it should be grouped with the lymphoblastomas. When a disease has been buffeted around for more than a hundred years there is some good reason why it has been attacked. We admit that it occasionally occurs in association with other diseases, but this does not justify its exclusion as a recognizable disease. We believe with Dr. Wile that it is a member of the group of lymphoblastomas.

Dr. C. Guy Lane, Boston: I wish to review briefly the blood picture in four cases which have come under our observation. One of the cases I have already discussed in this paper. The second case was clinically one of definite mycosis fungoides with large ulcerated tumors generally distributed. It was under observation for six months, and the white blood cell count varied from 24,000 to 59,000 with a lymphocyte count of from 70 to 80 per cent. The third case was also clinically one of definite mycosis fungoides and showed similar ulcerative nodules, the nodules being more profuse but smaller in size. The white cell count varied from 30,000 to 44,000. In this case the eosinophils varied from 9 to 48 per cent, the lymphocytes from 2 to 6 per cent, and the polymorphonuclears from 57 to 82 per cent. In the last case there was also a clinical diagnosis of mycosis fungoides, with ulcerative nodules of a more localized character. The pathologic diagnosis at autopsy was malignant lymphoma, with involvement of the skin, spleen, liver and retroperitoneal and axillary glands. In this case the white blood cell count varied from 38,000 to 103,000 and the lymphocytes were as high as 93 per cent.

At the Massachusetts General Hospital Dr. Greenwood and I have had some difficulty with both the roentgenologists and the pathologists in maintaining the diagnosis of mycosis fungoides. They are attempting to classify all the conditions of this group, and perhaps rightly, as lymphoblastoma, but at the same time we have continually to call their attention to the fact that mycosis fungoides is a definite clinical entity which is well known and has been discussed as such for years by dermatologists. It can be classed perhaps as a subgroup under lymphoblastoma, but we feel that the term should not be given up and should not be superseded by the term lymphoblastoma. I agree with Dr. Wile that in these cases it is perhaps

true that the low white cell count may be due to continued roentgenotherapy. I feel that this form of treatment is necessary, and in my experience it is the only thing that keeps the condition under control at all. Practically all of the patients at the Massachusetts General Hospital have been given a great deal of roentgenotherapy, and many of them have had a rather low white cell count. I have been interested in going over the slides in this case with one of the well known pathologists in Boston and in having him say that he thought it by no means out of the bounds of possibility for the conditions to be due to the same or to an allied factor in the circulation. At the beginning I felt that probably the changes in the skin and blood were coincidental, but as I have talked it over with others and considered the case more thoroughly, it has seemed possible to me that the condition may be considered as a link between the diseases in the lymphoblastoma group.

A VOLATILE SULPHIDE IN OINTMENT FORM

ELBERT CLARK, M.D.
EVANSTON, ILL.

Twelve years ago Pusey expressed to me the opinion that sulphur in volatile form incorporated into an ointment would be more useful in dermatologic conditions than precipitated sulphur.[1] After using such an ointment for ten years, I am able to verify this opinion. The volatile sulphide most used by me is solution of sulphurated lime N. F.

The ointment which I have found most convenient has the following formula:

	Gm. or Cc.
Solution of sulphurated lime	30
Anhydrous wool fat	40
Petrolatum	80
Pulverized camphor	1.5

The wool fat and petrolatum are melted and thoroughly mixed. When the mixture is cool, the solution of sulphurated lime is worked in. Pulverized camphor is next incorporated. The preparation has a deep yellow color and an odor similar to that of hydrogen sulphide.

This ointment may be used from one-half (for children) to full strength (for adults) in scabies. It destroys the parasites within twenty-four hours. There is seldom any irritation of the skin from the ointment. I advise each patient to rub the ointment thoroughly into the skin every twelve hours for three applications.

As a poultice it is effective in the early stage of furuncle.

For practically all other diseases of the skin for which sulphur is indicated, this ointment may be used, mixed with some suitable base, together with other drugs. In dermatitis seborrheica and in certain types of eczema, from 15 to 25 per cent is the strength of greatest usefulness. In the subacute stage of eczematoid dermatitis of the hands, approximately 20 per cent is the best strength.

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1. This seems entirely logical, and one would expect a more immediate action from sulphur in the form of a volatile sulphide ointment if the present theories of the action of sulphur are correct. Cushny (Cushny, A. R.: A Text Book of Pharmacology and Therapeutics, ed. 3, Philadelphia, Lea Brothers & Co., 1903) stated: "Sulphur is in itself inert. . . . Applied to the skin in ointment, sulphur appears to be formed in part to sulphide, particularly if some alkali be added." In the United States Dispensatory, edition 21, appears the statement: "When brought in contact with the skin, especially in the presence of alkalies, a . . . union of sulphur with hydrogen takes place as in the intestines. The alkaline sulphide thus formed is an active poison to various pathogenic parasites and sulphur is therefore a useful remedy in such diseases as scabies, ringworm, and favus. Besides this effect the sulphides by their local stimulating effect tend to overcome congestion in the skin and they have the power of softening the horny elements. . . ."

When resorcinol is mixed with this ointment, a volatile sulphide is freely eliminated. Thus in the treatment of tinea versicolor the affected areas are sponged with a 4 to 6 per cent alcoholic solution of resorcinol. The ointment is next rubbed into the skin. For seborrheic conditions of the scalp and in suitable cases of acne vulgaris a more watery cream is preferable. For use on the scalp, the formula is:

	Gm. or Cc.
Solution of sulphurated lime	15–20
Solution of calcium hydroxide	30–35
Anhydrous wool fat	17
Petrolatum	33

This cream should be applied liberally once or twice a week, rubbed in well and left in place for twenty-four hours. A stocking-cap is to be worn during this time.

For acne of the back in most males this formula will not be too strong. For acne of the face a weaker preparation is needed. The formula for this is:

	Gm. or Cc.
Solution of sulphurated lime	7.5–20
Solution of calcium hydroxide	30–42.5
Anhydrous wool fat	17
Petrolatum	33

Mix with equal parts of ointment of rose water. Apply once daily. The watery creams are much more difficult to prepare.

Odor is not an important objection to these ointments. Almost no odor remains ten minutes after application. The odor reappears when the patient bathes. This indicates that its action is prolonged and not momentary, as is the case with volatile sulphides in liquid form. When mixed with ointment of rose water the sulphide odor almost disappears.

I have kept some of this volatile sulphide ointment in an open jar for fourteen months. A thin layer at the top becomes oxidized so that it is nearly white. The sulphide odor disappears from this layer. Just beneath, the ointment is as yellow and pungent as when first made.

My experience with an ointment containing an acid volatile sulphide is not sufficient to justify a definite opinion as to its comparative usefulness. It seems to be a little more effective in seborrheic dermatitis.

In comparison one may say: A volatile sulphide in ointment form is immediately "available" when applied to the skin. Sulphur in ointment form, on the other hand, must be decomposed into a sulphide before it exerts therapeutic action. This phase of decomposition may account for the irritation of the skin which frequently follows the application of sulphur ointment. The sulphide ointment acts at once. In proper strength it is soothing.

636 Church Street.

HOT BATHS IN EXPERIMENTAL PRIMARY SYPHILIS OF RABBITS AND IN TRYPANOSOMIASIS OF RATS

JOHN A. KOLMER, M.D.
AND
ANNA M. RULE
PHILADELPHIA

About six years ago Schamberg and Rule [1] reported that the immersion of rabbits in hot water at 45 C. (113 F.) for from fifteen to twenty minutes three days after intratesticular inoculation with Spirochaeta pallida and daily thereafter for from eleven to seventeen days resulted in the complete sterilization of the animals, since syphilomas did not develop in the testicles and the inoculation of fresh animals with emulsions of the inguinal lymphatic glands failed to produce syphilitic infection. Later [2] it was observed in a single rabbit that, while these baths caused the healing of a secondary lesion, cure was not complete since transplantation of glands into a fresh animal resulted in infection.

In these experiments the whole animal was immersed in the hot water, with the exception of the head.

It occurred to one of us (J. A. K.) that the results may have been due to the local effects of hot water on the testicles rather than to the general elevation of body temperature, which averaged about 4 F.

With this in mind we have repeated the experiments in exactly the same manner, except that the inoculated testicles were kept out of the water each time the baths were given.

Six rabbits, along with several controls, were inoculated intratesticularly with the Nichols-Hough strain of Spirochaeta pallida, which was the same as that used by Schamberg and Rule.

Four days later four of these rabbits were immersed in hot water at 45 C. for twenty minutes in such a manner that the testicles (and of course the heads) were kept out of the water. The average elevation of rectal temperature was approximately 4 F. These baths were repeated

From the Research Institute of Cutaneous Medicine of Philadelphia.

1. Schamberg, J. F., and Rule, A. M.: Studies of the Therapeutic Effect of Fever in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **14**:243 (Sept.) 1926; The Therapeutic Effects of Hot Baths in Experimental Primary Syphilis in Rabbits, J. A. M. A. **88**:1217 (April 16) 1927.

2. Schamberg, J. F., and Rule, A. M.: The Effect of Extremely Hot Baths in Experimental Syphilis, Arch. Dermat. & Syph. **17**:322 (March) 1928.

daily for a total of fourteen days. In all four of the animals, as well as in the untreated controls, acute testicular syphilis developed in from eighteen to thirty days, and the presence of actively motile spirochetes was shown.

The remaining two rabbits were given the baths at the same time and in the same manner, except that the testicles were also immersed as in the experiments by Schamberg and Rule. In neither of these animals did testicular syphilis develop and transplants of lymph glands to fresh animals gave negative results, in confirmation of their observations.

The results indicate, however, that the sterilizing effect of water at 45 C. for twenty minutes is largely a local one on the infected testicles rather than the result of a general elevation of body temperature averaging about 4 F. during each treatment. In this respect the results are in agreement with those reported by Kolmer and Rule [3] on the effects of intravenous injections of typhoid-paratyphoid vaccine and Coley's fluid in the treatment of acute testicular syphilis of rabbits, since as many as ten doses at intervals of three days were without appreciable curative effects even though the elevation of body temperature was from 2 to 6 F. and lasted from one to four hours with return to the preinjection level in twenty-four hours. It may be that the elevation of body temperature of rabbits by hot baths or by the intravenous injection of bacterial proteins results in the destruction of some spirochetes, but certainly the results observed indicate that the local effects of hot water on the local syphilitic lesions are decidedly more curative.

Schamberg and Rule have also observed that the exposure of Spirochaeta pallida in a water bath at 41 C. (105.8 F.) greatly reduces its virulence or infectivity for the rabbit. We have found that Trypanosoma equiperdum is likewise quickly destroyed at this temperature when suspensions of rat's blood in saline solution are exposed, and have therefore thought it worth while to determine the effects of similar hot baths on rats inoculated with this organism.

White rats were inoculated subcutaneously with approximately 50,000 Trypanosoma equiperdum, this route of infection with a relatively small number of organisms being chosen in order to give the longest possible incubation period and thus the most favorable for the curative effects of hot baths. Four or five days later the organisms were found in the blood from the tail, and four controls died of trypanosomiasis in from seven to eight days after inoculation.

Immediately after inoculation and at daily intervals thereafter six of the rats were immersed in water at 45 C. for from three to six

3. Kolmer, J. A., and Rule, A. M.: Bacterial Protein Fever in the Treatment of Syphilis in the Rabbit, Arch. Dermat. & Syph. **24**:546 (Oct.) 1931.

minutes. At the end of this time the rectal temperatures were found to be elevated from 6 to 7 F. above normal.

While the temperatures of the rats were elevated more highly than was observed with rabbits, it was found impossible to keep the former immersed for twenty minutes as was done in the case of the latter, since a number of rats immersed for this time perished from the effects.

In every instance, however, trypanosomes appeared in the blood from the tails of the treated rats five days later, and all died of trypanosomiasis about eight days after inoculation, as was found true of the untreated controls.

The results have indicated, therefore, that the elevation of the body temperature of rats by from 6 to 7 F. for from three to six minutes immediately after inoculation with Trypanosoma equiperdum and at daily intervals thereafter had no appreciable influence on the course and duration of the resulting general trypanosomiasis.

SUMMARY

1. The complete immersion of rabbits, with the exception of the heads, in water at 45 C. (113 F.) for twenty minutes four days after intratesticular inoculation with Spirochaeta pallida and daily thereafter for fourteen days resulted in the prevention of testicular syphilis and in sterilization of the inguinal lymphatic glands.

2. Immersion, however, of animals in exactly the same manner with the exception that the testicles were kept out of the water did not retard or prevent the development of acute testicular syphilis with actively motile spirochetes.

3. It is suggested, therefore, that the sterilizing effects of hot baths on primary testicular syphilis of rabbits are largely local rather than due to a general elevation of about 4 F. of body temperature.

4. The immersion of rats immediately after subcutaneous inoculation with Trypanosoma equiperdum and daily thereafter in water at 45 C. for from three to six minutes with an elevation of body temperature of from 6 to 7 F. did not retard or prevent the development of fatal trypanosomiasis.

SYMMETRICAL LIVIDITIES OF THE SOLES

HOWARD J. PARKHURST, M.D.
TOLEDO, OHIO

In 1924, Pernet [1] described two cases of a condition which he called "symmetrical lividities of the soles of the feet." His first patient was a girl, aged 14, who had had scleroderma for eighteen months, for which thyroid extract had been administered, and who, during the following spring had chilblains about the tips of her fingers. The author noted that "her circulation was not good." The following autumn (Nov. 12, 1915) she presented:

> . . . acute symmetrical trouble about the soles in the shape of bluish-red patches, which had become paler in their central parts. The patches were slightly raised and had an edematous, blebby look, but contained no fluid. The borders of these patches were well defined.

The heels and the adjacent parts of the soles were involved. Pernet continues:

> Hyperidrosis of the rest of the soles was present. I came to the conclusion that the plantar condition was not connected with the morphea or scleroderma, but was a thing apart, probably of chilblainy or hyperidrotic origin. . . . What struck me most about the plantar condition was the symmetry of the affected areas.

Pernet's second patient, a boy, aged 14, presented an apparently identical symmetrical condition of two weeks' duration, which had begun on the plantar surface of the left heel. There was some hyperhidrosis. In the author's words, there were:

> . . . pale cyanotic lividities, slightly raised above the level of the skin and tailing off anteriorly and externally into a somewhat reddened border. . . . There was nothing else about the boy's skin.

As in the first case, the heels and adjacent parts of the soles were involved. In neither case did the distribution coincide with the innervation of the sole. Improvement followed the oral administration of sulphur and the local application of calamine lotion.

I have recently observed two cases apparently of this type.

REPORT OF CASES

CASE 1.—Miss E. K., a pupil nurse, aged 20, consulted me on Feb. 3, 1932, because of several slightly burning, dusky red patches the size of large and medium coins, arranged symmetrically on the heels. This condition was said to have been

1. Pernet, G.: Symmetrical Lividities of the Soles of the Feet, Brit. J. Dermat. **37**:123, 1924.

present for a year, and it was accompanied by hyperhidrosis, bromidrosis and bogginess of the soles. The legs showed no evidence of circulatory disturbances. There had been no previous disease of the skin, and there were no clinical signs of dermatophytosis. The possibility of toxic erythema was considered, but the general health was excellent, and there were apparently no foci of infection. The eruption bore some resemblance to dermatitis medicamentosa (fixed eruptions due to such drugs as phenolphthalein, antipyrine and arsenic), but there had been no previous medication. There was no history of frostbite.

The eruption disappeared completely in a week on the application of a 25 per cent solution of aluminum chloride twice daily, after washing. In April this treatment was stopped, and the condition recurred. However, it vanished promptly when the use of the astringent two days a week was resumed as a preventive measure, and there has been no recurrence.

CASE 2.—Frank H., a student, aged 21, had had no previous disease of the skin, except impetigo, for which I had treated him in 1930. There was no history of frostbite or apparent focus of infection, and no laxatives or other medication had been taken. When he consulted me on Feb. 21, 1932, there were on the heels symmetrical, discrete, slightly elevated, livid patches the size of a large coin. This condition was of a week's duration, and there were no subjective symptoms. Hyperhidrosis and bromidrosis were present, and there was slight scaling between the fourth and fifth toes of both feet. The patient was told to wash the feet night and morning and to sop on a 25 per cent solution of aluminum chloride; within a week the eruption had disappeared. The astringent is still being applied two days a week as a preventive measure, and the eruption has not recurred.

COMMENT

The eruption is symmetrical and consists of irregular, sharply outlined, slightly raised, bluish-red macules, the size of a coin and larger, located about the heels and the adjoining parts of the soles, of from a week's to a year's duration, with slight or absent subjective symptoms. Hyperhidrosis was present in every case, and in both of mine complete involution occurred after a week's employment of an astringent solution.

In my cases the eruption resembled that of erythema toxicum, dermatitis medicamentosa (fixed eruption due to phenolphthalein, antipyrine or arsenic) or frostbite. All of these possibilities were carefully excluded, and the exact symmetry of the eruption was a further argument against a diagnosis of pernio. In view of the response to treatment with aluminum chloride, it would seem that the hyperhidrosis was an important causative factor, perhaps dependent on some vasomotor abnormality.

A rather brief survey of the literature since 1924 reveals no reports of similar cases, and the only American textbook of dermatology which describes the condition is Sutton's.[2] Dr. Robert C. Jamieson, of Detroit, presented a case, in an intern, before the Detroit Dermatological Society in 1931, but unfortunately there was no clinical record, and it

2. Sutton, R. L.: Diseases of the Skin, ed. 8, St. Louis, C. V. Mosby Company, 1931, p. 387.

was not published in the proceedings. Treatment was not given, and the patient has left Detroit. Dr. Jamieson [3] also has had under observation another patient with this condition, a dentist, who gave a rather vague history of possible frostbite several years previously. In this case the eruption cleared up under applications of a 1 per cent solution of formaldehyde and a dusting powder; occasional mild relapses have occurred, with a similar response to treatment. Dr. Jamieson informs me that he has probably seen five or six cases, including those mentioned, and that hyperhidrosis was present in all. He feels that the hyperhidrosis is a probable predisposing or precipitating factor. These observations would lead one to suspect that the condition is possibly not rare, after all, and that it may often have passed unrecognized.

3. Jamieson, Robert C.: Personal communication.

TULAREMIA

A DISEASE OF INCREASING DERMATOLOGIC IMPORTANCE

A. J. MARKLEY, M.D.
DENVER

Prior to 1924, knowledge of tularemia was limited to fifteen cases observed and studied in the United States; since that time, however, the disease has been reported from practically every section of this country, the number of cases being about one thousand; in addition, it has been shown to occur in large numbers in Japan and Russia, and is probably of worldwide distribution.

Although not essentially a disorder of the skin, tularemia has attracted an active interest among dermatologists, as shown by the excellent papers of Miller and Taussig,[1] Shelmire,[2] Netherton[3] and Belote,[4] as well as by numerous more recent reports of cases. It is no longer to be regarded as a rare disease. The most frequently occurring clinical form of this condition, the ulceroglandular type, will certainly come increasingly to the attention of dermatologists, since it always begins as a lesion of the skin, a typical infective granuloma, which often closely resembles other disorders belonging in the category, and as such presents an interesting and important clinical and diagnostic problem.

There is a complete and excellent literature dealing with the historical, etiologic and clinical aspects of this disease, and in this paper it is intended only to emphasize further the frequency of its occurrence, its interest and importance to dermatologists, the increasing number of recognized animal and insect carriers and transmitters and the consequent extension of the field of necessary inquiry in determining the nature of conditions suggestive of tularemia.

Because of injuries incident to preparing them for use as food, wild rabbits are the principal sources of infection of human beings with tularemia; the disease is perpetuated among them by the transmission

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Read before the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 3, 1932.

1. Miller, H. E., and Taussig, L. R.: Tularemia, Arch. Dermat. & Syph. **19**:378 (March) 1929.

2. Shelmire, B.: Tularemia Resembling Sporotrichosis, Arch. Dermat. & Syph. **19**:918 (June) 1929.

3. Netherton, E. W.: Tularemia with Reference to Its Cutaneous Manifestations, Arch. Dermat. & Syph. **16**:170 (Aug.,) 1927.

4. Belote, G. H.: Tularemia, Arch. Dermat. & Syph. **23**:926 (May) 1931.

from animal to animal through the medium of biting and blood-sucking insects, which also frequently infect man and other animals.

Domestic rabbits are highly susceptible and are free from the disease probably only because they are free from lice and ticks and contact with wild rabbits; when running wild, however, they too may be the occasion of direct infection of human beings. Numerous other animals are now known to be naturally infected; of these, ground squirrels, rats and mice seldom come into direct contact with human beings; the sheep, the muskrat, the opossum and the woodchuck, however, are common contacts during removal of their skins or as food, and many instances of direct infection of human beings from these sources have been reported.

Certain game birds also have been shown to be either experimentally susceptible to tularemia or naturally infected by it, constituting another source of possible direct infection of human beings.

Indirect infection of human beings has occurred through the bites or scratches of nonsusceptible animals the mouth parts of which had been contaminated by the killing or eating of other animals with naturally acquired tularemia; in one instance, infection evidently occurred through playing with a dog which had recently killed ground squirrels.

Next to wild rabbits in importance as sources of infection of human beings with tularemia are ticks, deer flies and certain other insects which transmit the disease to both man and other animals through biting or blood-sucking or through the crushing of their bodies on the skin. Such infections are definitely seasonal in their incidence, corresponding with the period of activity in the life cycle of the insects.

Ticks constitute a permanent reservoir of infection, because they transmit the specific organism by heredity to their young and harbor it throughout their life in the intestinal tract. Francis [5] expressed the belief that infection following tick bite may be due to the contamination of the wound by feces, as the salivary glands do not contain the organism.

No doubt other sources of both animal and insect infection will be demonstrated as cases are reported and research is continued.

Although the eruptions of the skin observed in tularemia are such as may occur in the course of any acute infective process and are of no aid in diagnosis, the clinical history and other manifestations are often highly characteristic and justify a presumptive opinion; the determining factor in diagnosis, however, should always be a positive agglutination test. This positive test is highly specific; it apparently persists throughout life, and is accepted as evidence of permanent immunity. In the

5. Francis, E.: Harvey Lectures, Philadelphia, J. B. Lippincott Company, 1927-1928.

recently observed case of a woman who contracted tularemia in the seventh month of pregnancy, the blood of her infant two weeks after birth was positive in a dilution of 1 : 500. Cross-agglutination with certain other organisms may occur, but the titer is usually quite different. Some confusion might also arise in the diagnosis of other acute infections if a positive agglutination were discovered which resulted from previous tularemia.

Accumulating experience with, and observation of, cases of tularemia show that infection often occurs in unusual and unsuspected ways. The history may contain nothing suggestive; the lesions may simulate those of other infective granulomas, and diagnosis can be established only through the observations on the blood. Patients with such cases are most likely to come under the care of the dermatologist, and, as was expressed by Simpson,[6] the first consideration in the recognition of tularemia is "to have the disease in mind."

DISCUSSION

Dr. Fred D. Weidman, Philadelphia: It is an additional matter for concern that the domestic rabbit has now been incriminated as a carrier of tularemia, because the bedbug so often infests the rabbit hutch, in our laboratories, for example. Of course, the relationship of that parasite to both animals and man introduces the factor of transmission by animals, which is calculated to increase the incidence of tularemia.

Dr. Samuel Sweitzer, Minneapolis: At the University of Minnesota, Professor Green, has been working on this problem for several years and spends much time in the North woods counting ticks and other insects. This work has resulted in the demonstration that the disease is found in the Eastern wood tick, Dermacentor variabilis. These ticks feed on rabbits and undoubtedly get their infection from that source. Measurements carried out on the percentage of ticks infected have shown the disease to be present in about 0.1 per cent of the ticks. The percentage of infection is being measured each year to determine whether the hazard of human infection from this source increases when rabbits are abundant and are dying off.

It has also been found that the muskrat is very susceptible to tularemia, and this has led to the recognition of several cases of tularemia in Minnesota resulting from the handling of muskrats. Tularemia has also been found to be a disease of birds. Ruffed grouse were found to die of the natural infection, and a quail was found dead which had succumbed to this disease.

It is becoming apparent that tularemia is a disease that is widely distributed among wild animals and their tick parasites.

Dr. E. W. Netherton, Cleveland: Dr. Markley has very well stated that if one keeps in mind the possibility of this disease, one is not likely to overlook the diagnosis.

Types of the disease which he did not mention were subcutaneous nodules involving the lymphatics which have been reported as simulating sporotrichosis

6. Simpson, W. M.: Tularemia, New York, Paul B. Hoeber, Inc., 1929; J. Lab. & Clin. Med. **15**:311 (June) 1930.

and the typhoid type of the disease which has been reported as occurring in laboratory workers. The latter type does not have ulceroglandular manifestations, but there may be a generalized eruption which may roughly simulate the exanthems. In such cases care must be exercised in making a differential diagnosis.

DR. E. B. TAUBER, Cincinnati: I wish to agree with the statement of Dr. Markley that tularemia is becoming a dermatologic problem. In our section of the country, Dr. William Wherry, professor of bacteriology, of the Cincinnati General Hospital, reported the first case of tularemia in a human being, and the members of our department of bacteriology have developed both an agglutination serum and a skin test for tularemia. The substance is made of killed B. tularense, and after being used causes a definite and fairly accurate reaction within two hours in some instances and always within twenty-four hours. In this test the reaction takes the form of an elevated red wheal, 2 cm. square, with central involutions, which become cupped to some extent. The members of this department have also undertaken to abort tularemia through the use of a serum, but without success. They then used a convalescent serum in cases of tularemia, giving the patients increased doses, and rather striking results were obtained in shortening the duration of the infection. This work was done by Dr. Lee Fochat of the Cincinnati General Hospital.

A fact of historical interest is that Dr. William Wherry is the only man who has done a great deal of work with tularemia without acquiring the disease.

DR. H. J. TEMPLETON, Oakland: As a matter of historical interest, it might be recalled that this disease, which takes its name from the county of Tulare in California, was first described by a country practitioner, Dr. Pierce, in Utah. Several years ago he saw a number of these cases in Utah and described them under the title of "deer fly fever"; he recognized the importance of the deer fly in the transmission of the disease long before the exact etiologic agent had become known.

DR. ARTHUR J. MARKLEY, Denver: Regarding Dr. Weidman's comment, bedbugs certainly are carriers and may infect the domestic rabbits.

As Dr. Tauber brought out, laboratory workers have almost invariably become infected with the disease in laboratories in which investigation has been carried on, so that almost universally they decline to make biologic examinations to prove the diagnosis; however, that is no longer necessary, for agglutination tests are conclusive. The work on serum reported by Dr. Tauber is new to me.

The matter of convalescent serum was interesting, and I wrote to Dr. Francis, who replied that he had used it in only one case. Whether the serum was accountable or not is not known, but the patient recovered. Dr. Pierce wrote a paper on this subject and presented it before the Utah Medical Society twenty years ago, but before that time this disease developed in a young boy in California, who wrote a letter to his sister describing his symptoms so well that the letter may be regarded as a medical classic.

There is no specific treatment. Infected glands require incision and drainage, and other symptoms must be cared for symptomatically. The disease commonly has a long course.

DOSAGE OF SKIN THERAPY EXPRESSED IN INTERNATIONAL ROENTGEN UNITS

JOSEPH JORDAN ELLER, M.D.
AND
ARTHUR MUTSCHELLER, PH.D.
NEW YORK

A skin unit was proposed in electrical terms by MacKee as that dose which produced a definite erythema on human skin of average radiosensitiveness and a temporary epilation of the hair of the scalp. For many years this skin unit has been used almost universally as the unit dose in treatment with nonfiltered roentgen rays of the various superficial lesions of the skin and scalp. These electrical terms were proposed for one particular type of equipment; therefore it seemed advisable to translate these terms into such units of radiation as could be produced accurately and safely with the newer equipment and roentgen tubes.

The standard unit of roentgen dosage, called one roentgen is that dose which under normal conditions (0 C. and 760 mm. of mercury pressure) produces at saturation an ionization current of one electrostatic unit in a volume of 1 cc. of atmospheric air.

It appears advantageous to define therapy doses in roentgens, since roentgen tubes of different construction or origin, as well as different current generators of roentgen rays, may make the reproduction of the skin unit in electrical terms of spark gaps and milliamperes too inaccurate to be useful in more delicate and more carefully controlled work. Differences approaching 100 per cent in the radiation intensity may be found in tubes operated with a definite amount of electrical energy and without filters. These errors are caused by various compositions or thicknesses of the glass wall of the tube, or they may be due to deposits of anode material on the inner wall of the bulb caused by sputtering. This material is always a very effective filter, and large discrepancies in doses electrically defined may thus be well explained.

Then, also, as was verified in this investigation, it is known that the reaction of the human skin following the application of roentgen rays is not definite, accurate or standardized, and conditions of the skin, its individual susceptibility and the method of reading the reactions may all lead to errors. For these reasons it would seem advantageous to define so important a unit in terms of a more accurate and more reliable method of measurement.

The roentgen unit as a definition of radiation dosage is undoubtedly the more correct measure in which the average of the various doses

found clinically effective should be expressed. Through the courtesy of Drs. George MacKee, Fred Wise, George C. Andrews, Eugene Traub and the staff of the Skin Clinics of the New York Post-Graduate and of the Skin and Cancer hospitals, who have standardized their equipment clinically and have repeated their doses for a number of years, it has been possible to average these doses in the direction of the most probably correct value and to arrive at a measure in roentgens of this important radiation dose for skin therapy.

The doses given in the table were measured with a portable thimble roentgen dosimeter, which was carefully calibrated against a standard ionization chamber constructed on a fundamental centimeter-gram-second unit in full compliance with the physical requirements for the accurate definition of this unit as internationally defined and accepted (Dr. Mutscheller). The average of several readings is reported.

It is recommended that radiations be produced with a maximum voltage of 78 kilovolts, which corresponds to a peak of 97 kilovolts on

Average of Several Roentgen Doses for Skin Dose

Experimenter	Equipment	Roentgen Tube	Roentgens for Skin Dose
G. MacKee	Mechanical rectifier	Medium focus universal	312
J. J. Eller, 3 separate units	Valve tube rectifiers	Broad focus universal	335
Fred Wise	Mechanical and valve tube rectifier	Medium focus universal	356
Skin Clinic of the New York Post-Graduate Hospital	2 mechanical rectifiers	Broad focus universal	352
G. C. Andrews, 3 separate units	Mechanical rectifiers	Broad focus universal	290
E. Traub	Mechanical rectifiers	Broad focus universal	390
Stuyvesant Clinic, Skin and Cancer Hospital	Mechanical rectifiers	Broad focus universal	390
Average			340

the average standard sphere gap when measured on mechanical rectifiers. This voltage is to be measured either as the minimum wavelength voltage from a photographic spectrum or with electrical devices that do not include high frequency waves or surges superposed over the low frequency current.

CONCLUSIONS

1. The average value in roentgens of the MacKee skin unit has been measured on various apparatus, which had been calibrated clinically and had been in use for several years.

2. The average value for nonfiltered radiation producing in the majority of cases an erythema at a distance of 8 inches (20.32 cm.) is 340 roentgens (i. e., international roentgens).

3. The quality of roentgen radiation used should be produced by a maximum voltage of about 78 kilovolts.

4. Roentgen tubes that are too extensively blackened in use or have unusually heavy glass walls should not be employed to administer these doses.

100 West Fifty-Ninth Street.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

BUCCAL CARCINOMA. D. E. C. MEKIE, Am. J. Cancer **16**:971 (Sept.) 1932.

This essay is from the department of surgery, Edinburgh University. Predicating his work on the dictum that the treatment problem of buccal tumors is dependent on an intimate knowledge of their histology, the author presents a detailed histologic study of the normal tissues of the buccal cavity and tongue and an interpretation of their significance. It is emphasized that only the basal layer of epidermal cells possesses the power of reproduction, and that therefore all malignant processes in the epidermis have their origin in the basal cells and are subsequently modified by extrinsic and intrinsic factors. Most epidermal malignant conditions of the buccal cavity are termed acanthomas and are classified as papillary, nodular, ulcerative and fissured, the degree of malignancy usually being lowest in the papillary and highest in the fissured type. The process of keratinization in both normal and pathologic tissues is looked on as cellular degeneration rather than differentiation, and tumors showing the least tendency to undergo degenerative changes are the most malignant.

On a basis of characteristics in the growing margin of a carcinoma, the author recognizes three common types: (1) that in which the invading cells are in "club" formation, thrusting themselves downward without any tendency toward separation from the parent body, and with keratinization a common feature, (2) the "infiltrative" variety, in which the malignant cells break away from the main tumor mass and infiltrate as fine strands into and between the muscle fibers and connective tissue bundles, and (3) the group showing "en masse" growth of atypical basal cells with an absence of cell nest formations. The infiltrative type exhibits an anaplastic type of cell, shows little or no associated lymphocytic infiltration and appears to be the most malignant group. The "club" formation was commonest, being characteristic of 48 per cent of the cases studied. The infiltrative variety comprised 32 per cent.

Extension of buccal carcinoma from its point of origin is recognized as occurring by (1) direct local invasion, especially common in lingual cancer, (2) spread along fascial planes, where the fascia forms a barrier to penetration but favors parallel extension, (3) lymphatic spread, appearing first in the lymphatics of the neck, (4) blood spread, occurring as the result of ulceration of malignant cells from the perivascular lymphatics into the lumen of a blood vessel, (5) neural spread, either perineural or intraneural, (6) salivary gland involvement and (7) implantation growths, a very uncommon occurrence. Lymphatic spread is discussed in detail. Leukoplakia is discussed in detail, particularly as regards its histopathology. Subepithelial edema, lymphocytic infiltration and increased vascularity are considered to be the primary factors in the development of leukoplakia, with basal cell irregularity, mitotic activity and increase of the middle stratum of epithelium, with cellular edema and alteration of the cornified layers as secondary features.

XANTHOMA OF THE BREAST. C. D. HAAGENSEN, Am.J.Cancer **16**:1077 (Sept.) 1932.

The author reports three cases of primary xanthoma of the breast among nine hundred cases of tumors of the breast observed at the Memorial Hospital, New York. In these three cases the preoperative diagnosis had been carcinoma. In spite of the rarity of this form of xanthomatosis, the author, having found reference to only one case in the literature, advises consideration of the disease in all cases of tumors of the breast associated with diabetes, nephritis or hepatic disease. The

diagnosis rests on histologic study, and differentiation must be made from secondary xanthomatous degeneration, a not uncommon occurrence in true neoplasms of the breast, inflammatory processes such as chronic cystic mastitis, and traumatic fat necrosis.

As an introduction to his subject, the author presents an excellent analysis of the subject of xanthoma, which he divides into primary xanthoma and secondary xanthomatous degeneration. He draws attention to the frequent association of visceral lesions, particularly in the liver, spleen and meninges, in cases of cutaneous xanthoma. Among the primary xanthomas, which are all to be considered localized expressions of xanthomatosis due to disturbed lipoid metabolism, he differentiates and discusses xanthoma palpebrarum, xanthoma multiplex, xanthoma diabeticorum, solitary xanthoma tumors, erroneously called xanthosarcomas, and Christian's (Schüller-Christian's) disease. The last is a rare disease of early childhood characterized by defects in the membranous bones of the skull, exophthalmos and diabetes insipidus. Secondary xanthomatous degeneration is observed commonly in giant cell tumors of the aponeuroses, tendon sheaths and joint capsules, and also in neurofibroma, neurogenic sarcomas and ovarian cysts, and in the avascular, poorly nourished portions of tumors, chronic inflammations and scars. In all these cases it is assumed that there is an underlying hypercholesteremia.

LIPOMAS. F. E. ADAIR, G. T. PACK and J. H. FARRIOR, Am. J. Cancer **16**:1104 (Sept.) 1932.

The authors present a study of 134 patients with lipoma from the service of the Memorial Hospital, New York. They classify these tumors as (*a*) simple solitary lipomas, (*b*) multiple lipomas, (*c*) congenital diffuse lipomatosis (sometimes associated with diffuse cavernous hemangiomas), (*d*) degenerated lipomas, and (*e*) liposarcomas. They advance the thesis that multiple lipomas are neurogenic tumors, and draw the following analogies between multiple lipomas and multiple neurofibromas: (*a*) Both are of multicentric origin. (*b*) The symmetrical distribution of the tumors suggests a disturbance or defect of the central nervous system as a causative factor. (*c*) Multiple lipomas and neurofibromas have a similar regional localization, e. g., on the neck, scapula, popliteal space, arms, thighs and lumbar region. (*d*) Both conditions may be classified as intracutaneous, subcutaneous, fascial and visceral; multiple lipomas may appear in the lungs and liver where fat is normally absent. (*e*) Multiple lipomas and neurofibromas may exist in the same person. (*f*) The flat, coffee-colored pigmented macules of von Recklinghausen's disease are often observed in multiple symmetrical lipomatosis. (*g*) There is a hereditary or familial influence on the genesis of both multiple lipomas and neurofibromas. (*h*) Sensory and trophic disturbances are associated with both tumors as hyperesthesia, pain, hypesthesia and atrophy of the skin. (*i*) Painful scars are frequent following the extirpation of lipomas and neurofibromas. (*j*) Both varieties of tumors occur in young adults.

IS THE INCREASE OF CANCER REAL OR APPARENT? M. T. MACKLIN, Am. J. Cancer **16**:1193 (Sept.) 1932.

This presentation is based on a thorough analysis of the vital statistics of Canada, where the death rate from cancer per hundred thousand of population has risen from 46.8 in 1901 to 75 in 1921, and to 90 in 1929. The author states that the increase in cancer is not apparent but real, and that it is particularly evident in the age group over 60. The average age at which cancer claims its victims does not appear to be decreasing. The saving of lives after the cancer age has been reached has been perhaps the greatest factor in the increase of deaths due to cancer. The cancer rate might therefore justifiably be used as an index of the state of preventive medicine and sanitation in a country, since not only does preventive medicine bring more people to the cancer age, but it keeps them from dying of preventable causes after they get there, so that it is inevitable that the death rate from a few diseases, inclusive of cancer, not preventable at present, will mount.

End-Result of Cancer Cases Treated in Philadelphia Hospitals in 1923, as Shown by Special 1930 Follow-Up Studies. A. H. Estabrook, Am. J. Cancer **16**:1206 (Sept.) 1932.

This investigator of the research department of the American Society for the Control of Cancer secured a five year follow-up in 86 per cent of 1,802 cases in which a diagnosis of cancer was made in seven general hospitals. Of the total group under treatment, 10.6 per cent were alive in 1930, and of these 191 patients all but 21 were in good physical condition. The group with cancer of the skin showed the highest percentage alive, 22.2, or 55 of 248 cases. After deduction from this group of 53 patients for whom the end-result was unknown and 24 who died of conditions other than cancer, there remained a total of 165, 55 of whom were living and 110 of whom died of cancer, giving a survival rate of 33 per cent. When the group with cancer of the skin is deducted from the total, 8.8 per cent of the remaining 1,554 patients were found to be alive. The group with involvement of the buccal cavity showed 15 per cent alive in a total of 253 patients; this record was surpassed by the group with cancer of the bones which had a survival rate of 18 per cent. Ninety-three per cent of the deaths were from cancer, and of the survivors 29 per cent had cancer of the skin and 20 per cent cancer of the buccal cavity. Patients with cancer of the genitalia were not included in the group with carcinomas of the skin. Cancers of the lip were included as tumors of the buccal cavity, as were those of the tongue, mouth, tonsils, palate, jaw and parotid. Radiation treatment alone was employed in 810 cases; 12.5 per cent of the patients were reported to be alive, 73.3 per cent were dead, and the status of the remaining 115 was unknown. Surgical treatment alone was used in 336 cases, with 11.6 per cent of the patients surviving, and operation combined with other forms of treatment, mainly radiation, was used in 317 cases in which 13.9 per cent of the patients were alive. (It must be obvious that these figures, particularly as applying to cancer of the skin, concern a group of cases far less favorable for therapy than the general run of cases seen in private practice.)

Cell Resistance Incited by Radiation. Editorial, Am. J. Cancer **16**:1246 (Sept.) 1932.

Prime has shown by in vitro and in vivo experiments that repeated exposure of tumor cells to radiation does not render them resistant to the destructive action of radiation. The apparent reason why a cure cannot be obtained by the second irradiation when the first has failed is that the vascular effects which are responsible for so much of the necrosis of the parenchyma of the tumor are no longer obtainable, as the vessels are already damaged. If the irradiation is carried further, necrosis of the connective tissue only results, whereas the tumor cells still remain sufficiently resistant to escape the effects of the therapeutic doses. The phenomenon of radioresistance is therefore probably due not to the development of increased resistance in the cancer cells, but rather to the increased sensitiveness of the connective tissue.

Xeroderma Pigmentosum. M. M. Copeland and H. E. Martin, Am. J. Cancer **16**:1337 (Nov.) 1932.

The authors report four cases of xeroderma pigmentosum and discuss the subject in detail. They express the opinion that data at hand do not support the contention that a photodynamic substance, such as hematoporphyrin, is a causative factor, and endocrine disorders and trophoneuroses are ruled out.

Tobacco Tar: An Experimental Investigation of Its Alleged Carcinogenic Action. E. Bogen and R. N. Loomis, Am. J. Cancer **16**:1502 (Nov.) 1932.

The authors conclude from their experiments on the skin of mice and rabbits that the cutaneous application of the tar derived from the destructive distillation

of tobacco does not possess the irritating and epithelial-stimulating properties that lead to the production of neoplastic growths. Positive results were obtained on control animals with gas house tar.

THE TAR IN CIGARETTE SMOKE AND ITS EFFECTS. W. D. MCNALLY, Am. J. Cancer **16**:1515 (Nov.) 1932.

The smoking of a cigaret yields a tarry residue of from 5 to 15 per cent, of which from 6.5 to 11.5 per cent may be absorbed or retained in the body. This tar contains nicotine, phenolic bodies, pyridine bases and ammonia, irritants which account for leukoplakia, chronic bronchitis and possibly pulmonary cancer. The last 2 cm. of a burning cigaret retains most of the tar and other products of incomplete combustion; cigarets should therefore not be smoked when they are too short. Attempts to produce malignant growths in rats with the water-soluble products of cigaret smoke and with cigaret tar gave negative results.

HELIOTROPISM OF CHOLESTEROL IN RELATION TO SKIN CANCER. A. H. ROFFO, Am. J. Cancer **17**:42 (Jan.) 1933.

The author believes that there is a direct relationship between the cholesterol content of cutaneous tissue, exposure to sunlight and predisposition to malignancy. By experiments on animals he demonstrated an increase of cholesterol in areas of skin exposed to sunlight or to ultraviolet light. He determined that the cholesterol content of the skin of the face is from three to six times greater than that of the skin of the abdomen, and that it is higher in the exposed portions of the face, such as the nose and malar areas, than in shaded portions, as the forehead. Roffo observed that skin cancer occurs with greater frequency in those areas of the face showing the highest cholesterol content, and concluded that cholesterol prepares the soil for a subsequent malignant growth by acting as an accumulator of light.

EFFECTS OF NEO-ARSPHENAMINE IN SPONTANEOUS BREAST TUMORS OF MICE. W. C. HUEPER and S. ITAMI, Am. J. Cancer **17**:106 (Jan.) 1933.

Experiments conducted in the Cancer Research Laboratories of the University of Pennsylvania demonstrated that the growth of spontaneous mammary cancer in mice was stimulated by prolonged medication with neoarsphenamine. The authors advise against medication with arsphenamine in syphilis complicated by cancer because of the danger of injury interfering with the important process of lactic acid utilization by the liver in malignant tumors, the decrease of arsphenamine tolerance following roentgen irradiation, and the additional vascular effects of arsphenamine and the roentgen rays. H. R. FOERSTER, Milwaukee.

CONGENITAL SYPHILIS; RESULTS OF EARLY TREATMENT. E. D. ATLEE and R. M. TYSON, Am. J. Dis. Child. **44**:718 (Oct.) 1932.

In an article rather difficult to abstract, the following conclusions were reached by the authors: 1. Only occasionally does a baby show clinical evidence of congenital syphilis during the two weeks of the lying-in period. 2. A positive Wassermann reaction of the cord blood is sufficient evidence to warrant the giving of antisyphilitic treatment early. 3. A negative Wassermann reaction of the cord blood in a child whose mother is definitely syphilitic, although treated during pregnancy, is not sufficient evidence that the baby will escape congenital syphilis. 4. Our experience demonstrates that early treatment of congenital syphilis continued for fourteen weeks gives a high percentage of cures.

NEUROFIBROMATOSIS OF THE BLADDER. I. H. KASS, Am. J. Dis. Child. **44**:1040 (Nov.) 1932.

A case of cutaneous neurofibromatosis in a boy, aged 7 years, associated with an extensive neurofibromatosis of the urinary bladder was reported by the author. The pertinent literature was reviewed. ANDERSON, Los Angeles.

PELLAGRA: IMPROVEMENT WHILE TAKING SO-CALLED "PELLAGRA-PRODUCING" DIET. T. D. SPIES, Am. J. M. Sc. **184**:837 (Dec.) 1932.

In the six cases reported in this paper, all the symptoms of typical pellagra were present. A diet consisting of carbohydrate 1,700 calories, protein 110 calories and fat 400 calories was given until the cutaneous lesions had cleared up. Vitamins C, D and G were much restricted in the foods given, and were considered to be less adequate for normal nutrition than Goldberger's "pellagra-producing" diet. With one exception the lesions improved rapidly, the skin becoming practically normal by the third week. The results of this experimental diet led the writer to consider the influence of some secondary factor in the development of pellagra. He does not recommend the indiscriminate administration of this diet for any length of time in the treatment of pellagra.

THROMBO-ANGIITIS OBLITERANS AMONG WOMEN. B. T. HORTON AND G. E. BROWN, Arch. Int. Med. **50**:884 (Dec.) 1932.

The cases presented here are, in the opinion of the authors, the first to be recorded in women. In considering the possible explanation of the high incidence in men, they mention foci of infection (prostate or seminal vesicles), an endocrine basis, tobacco and the probably milder form in women.

SYNDROME OF ANEMIA, GLOSSITIS AND DYSPHAGIA: REPORT OF EIGHT CASES WITH SPECIAL REFERENCE TO OBSERVATIONS AT AUTOPSY IN ONE INSTANCE. M. M. SUZMAN, Arch. Int. Med. **51**:1 (Jan.) 1933.

In a review of these cases presenting the "Plummer-Vinson syndrome," the chief changes of dermatologic interest were the definite histologic abnormalities in the mucosa and muscle of the tongue and esophagus. These changes consisted chiefly of epithelial hyperkeratinization with areas of desquamation and degenerative atrophic changes in the underlying muscle. The condition did not appear inflammatory, although the submucosa showed a moderate degree of infiltration with lymphocyte-like cells. The appearance of some areas of the mucous membrane simulated leukoplakia. JAMIESON, Detroit.

LEPROSY OF THE EAR, NOSE AND THROAT. F. J. PINKERTON, Arch. Otolaryng. **16**:469 (Oct.) 1932.

This article is essentially a statistical study of about two hundred cases of leprosy, with lesions of the ear, nose and throat. Fifty per cent of the patients were found to have lesions on the face. Of those with lesions on the face, 63 per cent had lesions of the nose and alae, and many had involvement of the lips. The characteristics of the lesions as they occur in the ear, nose and throat are described. The favorite sites for the location of the organisms are the nose and external ear. In the nose serum is expressed from the mucous membrane by a steel blunt dissecting elevator applied just behind the mucocutaneous juncture on the septum. In this way one avoids the mistaking of the lepra bacilli for other acid-fast organisms in the nasal secretions. In snipping an ear, the area should be grasped firmly so as to produce ischemia of the part; a niche is made through the corium with a razor blade, and the blade is twisted in the tissue so

that it will carry away fluid free from blood cells. It is often necessary to carry out repeated examinations to establish a diagnosis. The article is rich in illustrations, and the author discusses the various methods of treatment of lesions of the ear, nose and throat.

RATTNER, Chicago.

PERLÈCHE: A CONSIDERATION OF ITS ETIOLOGY AND PATHOLOGY. M. H. GOODMAN, Bull. Johns Hopkins Hosp. **51**:263 (Nov.) 1932.

From a study of a case of chronic perlèche in an adult, associated with a typical erosio interdigitalis blastomycetica, and a case of acute perlèche in a child, Goodman concludes that a specific etiology of perlèche has not been determined. From a survey of the literature and the cultural studies from the two cases, it was suggested that perlèche might be primarily produced by streptococci, staphylococci or a fungus. He suggests the possibility, however, that an as yet undiscovered virus might be the primary agent, and that these organisms are secondary invaders. The article contains a rather detailed histologic account, which is about the only one in the literature.

ANDERSON, Los Angeles.

ERYTHEMA NODOSUM IN UNDERGRADUATE NURSES AND ITS RELATIONSHIP TO TUBERCULOSIS. JOHN T. CRUISE, Canad. M. A. J. **27**:603 (Dec.) 1932.

A study of thirty-three cases of erythema nodosum in undergraduate nurses showed that in seven (21 per cent) definite diagnosable pulmonary tuberculosis developed and that in four the condition was suspected, at the time of the rash or within six months. This proportion is large enough to suggest strongly a relationship between erythema nodosum and tuberculosis. Five of the nurses who could not be regarded as tuberculous had accompanying focal infections in the teeth, tonsils or sinuses, and it was found that in one there was a recurrence of the nodes when the infection recurred. Over half of the series had erythema nodosum during or after their affiliation with an institution for treatment of tuberculosis. Four of the cases are referred to in detail, and the pertinent literature is reviewed.

RATTNER, Chicago.

STUDIES ON THE PHYSIOLOGICAL EFFECTS OF FEVER TEMPERATURES: II. THE EFFECT OF REPEATED SHORT WAVE (30 METER) FEVERS ON GROWTH AND FERTILITY OF RABBITS: III. THE THERMAL DEATH TIME OF SPIROCHAETA PALLIDA IN VITRO WITH SPECIAL REFERENCE TO FEVER TEMPERATURES: IV. THE HEALING OF EXPERIMENTAL SYPHILIS LESIONS IN RABBITS BY SHORT WAVE FEVERS. R. A. BOAK, C. M. CARPENTER and S. L. WARREN, J. Exper. Med. **56**:725, 741 and 751 (Nov.) 1932.

In this series of articles are recorded the interesting results of raising temperatures artificially and the effects obtained on growth and fertility of rabbits and on Spirochaeta pallida. Treated rabbits were found to be just as fertile as untreated, but in general gained more weight and were apparently healthier. In determining the effect of fevers on the infectivity of Spirochaeta pallida, observations were recorded on development of inoculation lesions, dark-field examination, Wassermann tests and reinoculations. The length of time required to kill the spirochete varied according to the temperature, being five hours at 39 C., three hours at 40 C., two hours at 41 C. and one hour at 41.5 C. In inoculated rabbits, one exposure of six hours at 41 C. to 41.5 C. was found to be as effective as a series of twenty to thirty periods of fever produced by short wave radiation, regardless of the size or type of the testicular lesion. Dark-field examination of lesions in treated rabbits always gave negative results. The fever treatment was found to be effective at any period of experimental syphilis in rabbits.

JAMIESON, Detroit.

CHEMICAL COMPOSITION OF THE ACTIVE PRINCIPLE OF TUBERCULIN: XVI. LOCAL CUTANEOUS SENSITIZATION (ARTHUS' PHENOMENON) PRODUCED IN NORMAL RABBITS AND GUINEA-PIGS BY THE PROTEIN OF TUBERCULIN. FLORENCE B. SEIBERT, J. Infect. Dis. **51**:383 (Nov.-Dec.) 1932.

There has been a controversy as to whether animals could be specifically sensitized to tuberculin by repeated injection of any of the fractions of the tubercle bacillus without the presence of actual infection. Seibert found that specific cutaneous sensitization can be produced in normal rabbits and guinea-pigs by repeated injections of the highly purified, undenatured protein of tuberculin. This sensitization is of as high degree and of the same type as that produced by infection with live tubercle bacilli or by injection of dead bacilli. The most successful method for preparing and purifying the protein of tuberculin in such a way as to preserve its antigenic capacity she found was precipitation by means of ammonium sulphate or trichloracetic acid, or merely concentration and washing by means of ultrafiltration.

ISOLATION AND DIFFERENTIATION OF TUBERCLE BACILLI ON THE BORDET-GENGOU AND LÖWENSTEIN MEDIUMS. LUCY MISHULOW, J. Infect. Dis. **51**:416 (Nov.-Dec.) 1932.

The object of this study was to find a medium that could be easily prepared and stored, that would grow tubercle bacilli easily and rapidly, and that would give such characteristic growth for the different types that it could be used to differentiate them without resort to inoculation of animals. Bordet-Gengou medium was found excellent for isolation and cultivation of human and bovine types of tubercle bacilli. The author feels that the Bordet-Gengou medium might be substituted for animals in the isolation of both types. Löwenstein's medium was equally favorable for isolation of the human type of tubercle bacilli, although it is entirely unsuitable for isolation of the bovine type, as the latter failed to grow in primary cultures. By using both Bordet-Gengou and Löwenstein mediums, human and bovine types of tubercle bacilli could be differentiated by their growth characteristics. Avian tubercle bacilli grow rapidly and luxuriously on both mediums, giving distinctive rough and smooth colonies.

B C G gave such characteristic growth on these mediums that it could be differentiated from typical human and from typical bovine strains by the morphologic differences of the colonies. Plating on the Bordet-Gengou and Löwenstein mediums, therefore, may be used as an additional safeguard in preparing B C G vaccine. The Bordet-Gengou medium is especially advantageous because the glycerin-potato agar can be prepared and stored for many months. The necessary amount can be melted and mixed with sterile blood at the time it is needed, thus giving fresh plates whenever needed.

LATENT PERIOD IN PASSIVE ANAPHYLAXIS. JULIAN H. LEWIS, J. Infect. Dis. **51**:519 (Nov.-Dec.) 1932.

The present report of experimental data is concerned with the support of the cellular theory of anaphylaxis as against the humoral one. Freidberger found that the latent period in passive anaphylaxis could be dispensed with by using the homologous sensitizing antiserum, but Lewis could not confirm this. With the use of a guinea-pig antituberculoprotein serum of high titer, guinea-pigs could be passively sensitized to a fatal anaphylactic death in not less than four hours after the injection of the sensitizing serum, the same period required for sensitization with a heterologous antiserum. The smooth muscle of the uterus showed anaphylactic sensitization two hours after an intravenous injection of homologous sensitizing serum. An isolated uterus was passively sensitized after remaining in a solution of guinea-pig antituberculoprotein serum for two hours. The uterus was not sensitized after four hours in a solution of rabbit antihorse serum.

BEHAVIOR OF BACTERIOPHAGE IN BODY FLUIDS AND IN EXUDATES. M. G. COLVIN, J. Infect. Dis. **51**:527 (Nov.-Dec.) 1932.

A controversy has sprung up as to whether bacteriophage modifies the bacterium in the living body in a way comparable to that observed in the test tube. That the nature and extent of this process may not be identical with what is seen in vitro has been obvious, and several investigators have studied the effects of body fluid and tissues on the lytic process. The author found that there is a nonspecific inhibitory effect of serum on bacteriophagy, which was first observed and reported by Gratia. This phenomenon, first associated with the lysis of staphylococci, has been shown in connection with other organisms by subsequent investigators. In this report, the results of further investigations in regard to the importance of the various factors concerned in inhibition of bacteriophagy in body fluids are outlined. It has been found that variations of serum, body fluid, race of bacteriophage and bacterial strain or species introduce distinct differences in the amount of inhibition.

Attempts to adapt a staphylococcic or a streptococcic phage to produce complete lysis in serum have been practically unsuccessful. It is shown that repeated contact with serum may have a tendency to make an organism lysis-resistant, and consequently an adaptation to resist lysis develops. A study of the mechanisms of inhibition to lysis shows that serum delays multiplication of the bacteriophage, but does not prevent specific fixation of the corpuscle. In the serum, the protein fraction is the main factor in inhibition of lysis, while in the urine the crystalloid fraction inhibits. The findings suggest that bacteriophagy in the body is much modified as compared to test tube standards of lysis. The modification is in the direction of lessening the sterilizing capacity of the bacteriophage.

RESULTS OF EXAMINATION OF BLOOD FOR TUBERCLE BACILLI BY LÖWENSTEIN'S CULTURE METHOD. WEBB HAYMAKER, WALTER EKHARD and JULES FREUND, J. Infect. Dis. **51**:562 (Nov.-Dec.) 1932.

Recently Löwenstein published numerous reports on the presence of tubercle bacilli in the blood stream. According to him, they can be demonstrated regularly in the blood not only in miliary or far advanced pulmonary tuberculosis but in all forms of the disease and in certain other diseases hitherto not considered of tuberculous origin. For example, he reported that in about 50 per cent of cases of rheumatic fever tubercle bacilli were found in the blood stream. These remarkable conclusions are based on demonstrations of tubercle bacilli, not by animal inoculation, but by a cultural method developed by him for this purpose.

With Löwenstein's culture method, the author could not obtain any growth of tubercle bacilli from thirty-eight samples of blood from tuberculous patients. In four cases of polyarthritis, three of rheumatic heart disease and one of chorea, no tubercle bacilli were found in the blood either by culture or by inoculation of guinea-pigs.

CORNBLEET, Chicago.

TWENTY YEARS OF SYPHILIS UNDER SALVARSAN. C. MORTON SMITH, New England J. Med. **207**:159 (July 28) 1932.

Morton Smith reviews twenty years' treatment of syphilis with arsphenamine preparations. During this time the drug has been the chief factor in decreasing the incidence of both acquired and congenital syphilis, although much help has been given by prenatal clinics, social service and follow-up. The drug affords prompt healing of early infectious lesions, a result of great importance to the patient and his contacts. The author emphasizes the extreme importance from a public health point of view, and points to the marked improvement in the treatment of neurosyphilis which has taken place under the use of this agent.

Experience has shown that the therapeutic value of arsphenamine is much greater when supplemented with mercury or bismuth. The author calls attention to the trend toward slightly smaller doses and continuous treatment for two years at least. The value of the drug has been demonstrated in the review of a

thousand cases of interstitial keratitis and in the latent cases detected at prenatal clinics. The importance of early diagnosis and adequate treatment by arsenic supplemented by mercury or bismuth as a means of conserving and prolonging human life is stressed. The paper sums up a very extensive experience with this disease.

PAROXYSMAL HEMOGLOBINURIA. FRANCIS P. MCCARTHY and ROBERT WILSON, JR., New England J. Med. **207**:1019 (Dec. 8) 1932.

The authors describe two cases of paroxysmal hemoglobinuria—one occurring in early acquired syphilis and the other in early congenital syphilis. These were the only two cases seen in the 3,368 under observation during the past eleven years. In the congenital case, a familial tendency was shown by the demonstration in the blood serum of two younger sisters of the presence of an autohemolysin, in accordance with the earlier statement of Donath and Landsteiner. The Wassermann tests were negative in these persons. The spontaneous attacks disappeared promptly after antisyphilitic treatment was begun. In the acquired case, the spontaneous attacks of hemoglobinuria began only four years after the initial lesion, when the patient was 21. He has had no attacks since treatment was started.

LANE, Boston.

INFECTIVE ECZEMAS OF THE SCALP. G. B. DOWLING, Brit. M. J. **2**:830 (Nov. 5) 1932.

This paper deals briefly with the clinical characteristics and treatment of impetiginous eczema, "fausse teigne amiantacée" of Alibert, and seborrheic dermatitis. Seborrheic eczema frequently becomes impetiginous, and the two conditions are to be differentiated on clinical judgment in which the past history is important. The history of primary fissures in the postauricular folds of impetigo of the scalp, of previous attacks in childhood of eczema of the ears and scalp or of the presence of chronic blepharitis dating from childhood points to the diagnosis of microbic eczema, while the presence of seborrheic eczema on parts other than the scalp may be taken as presumptive evidence of primary seborrheic eczema.

VARICELLA IN OLD AGE. J. D. ROLLESTON, Brit. M. J. **2**:1007 (Dec. 3) 1932.

A case of varicella is reported in a woman, aged 76. In the years 1926 to 1932, the author observed twenty-nine cases of chickenpox in patients aged 18 years and upward. Of these only three were more than 30 years of age; there were two men, aged 31 and 64 years, respectively, and the woman of 76, whose case is reported in detail.

MONILETHRIX. J. GOODWIN TOMKINSON, Brit. M. J. **2**:1009 (Dec. 3) 1932.

Tomkinson records twenty-two cases of monilethrix in five generations of one family. He personally examined seventeen of the patients, and he saw portraits of four of the remaining five. Some interesting observations were made. The sexes were involved about equally. In the later generations there had been an increase in the frequency of incidence of the condition. In the third generation the percentage was 5.88; in the fourth, 40, and in the fifth, 54.16. The extent of involvement of the scalp varied from almost complete baldness to involvement of only the suboccipital region and the extreme frontal region. One youth, at the age of 14, with the advent of puberty, showed an improved growth of hair. The onset in some cases was as early as the sixth month. Two children were born with hair, which faded away at the age of 6 months, and this was followed by keratosis pilaris. Ten of eleven children in the fifth generation had keratosis pilaris of the scalp. All of the hairs were not affected from root to extremity. One pubic hair was affected in only a part of its length. In some of the hairs there was a concentration of pigment in areas composed of contiguous halves of nodes and internodes. These and many other interesting facts are brought out in the paper.

RADON VERSUS RADIUM: A PRELIMINARY REPORT. H. H. MCCOY, M. J. Australia **2**:232 (Aug. 20) 1932.

Twenty-eight patients with epitheliomas were treated with implants of radon (filtered with 0.5 mm. of nickel), and twenty-four patients with similar conditions were treated with radium needles (filtered with 0.5 mm. of platinum). The radon was found to be far from satisfactory. Delayed healing and radionecrosis had been observed in an unduly large proportion of cases, and the scars, even in favorable cases, too frequently have been large and unsightly.

ACHLORHYDRIC ANEMIA AS A CAUSE OF PRURITUS VULVAE OF SO-CALLED NEUROTIC ORIGIN. BRIAN H. SWIFT, M. J. Australia **2**:541 (Oct. 29) 1932.

The author was consulted by a woman for an intractable pruritus vulvae of so-called neurotic origin; she was a typical "nervous wreck." After an exhaustive study she was found to have a secondary anemia of chlorotic type, and a test meal revealed no free hydrochloric acid. Large doses of iron and dilute hydrochloric acid gradually improved the condition. The author has since encountered similar findings in several other cases, three of which are reported in detail. It was found also that in most of the cases the onset coincided with pregnancy.

RATTNER, Chicago.

CULTURE OF TUBERCLE BACILLI FROM CIRCULATING BLOOD BY LÖWENSTEIN'S METHOD AND SIMULTANEOUS TISSUE CULTURE IN TUBERCULOSIS OF THE SKIN. T. BENEDEK, Dermat. Wchnschr. **95**:1641 (Nov. 12) 1932.

In four cases of tuberculosis cutis luposa, one of tuberculid and two of lupus erythematosus, tissue cultures by the method of E. Keil and blood cultures by Löwenstein's method were made. Tubercle bacilli were obtained in the tissue cultures from the four cases of lupus vulgaris but not from the others. One blood culture from one case of lupus vulgaris was positive for tubercle bacilli. A subsequent culture was negative. The growth from the tissue cultures was abundant in the positive instances and was readily carried into subcultures. The blood culture grew sparsely, and the organisms lost their typical shape and acid-fast qualities in subcultures.

IMPORTANCE OF SPINAL FLUID FINDINGS IN THE PATHOLOGY OF LATENT AND CONGENITAL SYPHILIS. V. KAFKA, Dermat. Wchnschr. **95**:1650 (Nov. 12) 1932.

The author made quantitative studies of the albumin in the spinal fluids of patients with latent and congenital syphilis. He determined the globulin, albumin and total albumin content, and believes that an increase in the globulin alone probably indicates a previous syphilitic meningitis. This may occur when all other findings are negative. An increase in the albumin alone also occurs, but there is no satisfactory explanation for this finding.

AN INDUSTRIAL STIGMA OF LOCOMOTIVE ENGINEERS AND FIREMEN NOT PREVIOUSLY DESCRIBED. M. OPPENHEIM, Dermat. Wchnschr. **95**:1674 (Nov. 19) 1932.

The author observed a locomotive engineer with linear pigmented scars over his shin bone. These had resulted from frequent scratches inflicted when the patient climbed into the cab of the engine, especially in winter. Thirty other engineers and firemen who had had a number of years of service were examined, and the same scars were noted in varying degree in all. It is possible that the high frequency of the malignant conditions of the legs of persons in this occupation is due in part to trauma rather than to heat alone, as previously thought.

TREATMENT OF SKIN DISEASES, PARTICULARLY SCLERODERMA, BY MEANS OF FUMIGATION WITH IODINE. M. BREITMANN, Dermat. Wchnschr. **95**:1678 (Nov. 19) 1932.

The author treated three patients with scleroderma of the hands and forearms by exposing the affected areas to the gas formed by heating iodine crystals. The treatments were given every five or six days for from one to three months. All the patients were greatly benefited. He also obtained good results in some cases of vitiligo and in weeping eczema and furunculosis.

THORIUM X IN PARAPSORIASIS EN PLAQUES. KARL PREIS, Dermat. Wchnschr. **95**: 1680 (Nov. 19) 1932.

The author cleared up the lesions of two patients with parapsoriasis in a few days by rubbing them with a solution of thorium X in propyl alcohol.

A CASE OF SYPHILIS CONGENITA TARDA. JOHANNES JOST, Dermat. Wchnschr. **95**: 1687 (Nov. 19) 1932.

A gummatous glossitis developed in a boy, aged 19 years. The history excluded the likelihood of acquired syphilis. The Wassermann test and other blood tests were positive. There were no other stigmas of congenital syphilis.

COMPLEMENT-FIXATION REACTION WITH THE TUBERCULOSIS ANTIGEN OF WITEBSKY, KLINGENSTEIN AND KUHN IN LEPROSY. J. BRANTS, Dermat. Wchnschr. **95**: 1688 (Nov. 19) 1932.

The complement-fixation reaction with the tuberculosis antigen of Witebsky, Klingenstein and Kuhn gave positive results in fifty cases of nodular leprosy, in four of the mixed type and in twenty of twenty-six cases of nerve leprosy.

TECHNIC OF INJECTION INTO VARICOSE VEINS. F. A. SCHMIDT, Dermat. Wchnschr. **95**:1718 (Nov. 26) 1932.

The author has devised a connector by which he couples two syringes, connected with a single needle. One syringe is filled with the obliterating medication. After tourniquets have been placed above and below the varicose area, the needle is introduced into the lumen and the empty syringe used to aspirate the blood. The adaptor is then turned and the desired solution injected.

MAXIMAL TREATMENT OF PRIMARY AND SECONDARY SYPHILIS. RUDOLF STREMPEL, Dermat. Ztschr. **65**:1 (Nov.) 1932.

The author reviews the principal features of the maximal mixed treatment of Hoffmann and discusses its advantages. He includes a table showing in outline the treatment by this method of sixty-four patients with primary and secondary syphilis. They had been followed for periods ranging from three to eighteen years and had remained clinically and serologically well. Of this group, forty-seven had shown manifest secondary syphilis. Ten cases of early syphilis in which a relatively intensive course of treatment had failed to produce permanent cures are presented in tables and the reason for the failure in each case is discussed. Spinal fluid is obtained at the Bonn clinic by cisternal puncture preferably.

KERATOTIC DESTRUCTION OF PAPILLARY RIDGES IN DISSEMINATED KERATOSES OF PALMS AND SOLES. GUSTAV HOPF, Dermat. Ztschr. **65**:12 (Nov.) 1932.

Four cases of disseminated keratosis of palms and soles are described. By means of prints made by inking the surface of the palm and pressing it on paper, the author shows that the earliest lesions consist of small circumscribed areas of destruction of the papillary ridges. These small depressions are considered to be the primary lesions of the condition, and it is especially noteworthy that they do not occur around the follicular orifices. L. TAUSSIG, San Francisco.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

LOUIS CHARGIN, M.D., *Secretary*

Regular Meeting, Oct. 4, 1932

A. BENSON CANNON, M.D., *Chairman*

DERMATITIS EXFOLIATIVA (WILSON-BROCQ). Presented by DR. HERMANN FEIT.

W. B., a man, aged 70, born in England, who had lived in the United States for twenty-one years, had worked as a hairdresser, a piano polisher and a pipe fitter. The eruption had existed intermittently for more than thirty years, each outbreak lasting for from six months to one year. The eruption had begun with red spots on the eyelids. These were swollen and were covered with fine scales; from there the eruption had spread to the face, neck, chest and rest of the body, involving the whole integument gradually. The whole skin was reddened and very hot. Chills had become prevalent. The skin was always dry and scaly, with occasional weeping in a few spots. The sensation was more that of burning than of itching.

The patient appeared to be fairly well nourished, and the whole cutaneous surface was found to be reddened, thickened and covered with flaky scales which were dry except when the patient perspired. The perspiration had greatly diminished in comparison with what it had been in former years. The inguinal glands were very large. The hairs were dry, thin, lusterless and scarce. The nails were normal. There was no evidence of tuberculosis or leukemia. Most of the teeth had been removed without apparent influence on the cutaneous condition. Contact with heavy metals, such as arsenic and mercury, could not be proved. Atrophy was not present. The urinalysis gave negative results for sugar and albumin. There was no previous history of eczema or psoriasis.

DISCUSSION

DR. SIGMUND POLLITZER: Why is this condition presented as being of the Wilson-Brocq type rather than that of Hebra?

DR. HERMANN FEIT: In the Hebra type there is always atrophy. The duration of the disease and the general condition rule out this possibility.

DR. SIGMUND POLLITZER: The atrophy occurs rather late in some cases. This patient has had the condition for thirty years, which would seem to be long enough. However, a slight degree of atrophy is noticeable about the eyes. If he lives another thirty years he will have ectropion of the lid.

DR. FRANK C. COMBES, JR.: I agree with Dr. Pollitzer regarding the diagnosis. There is considerable suggestion of atrophy of the skin. My conception of the Wilson-Brocq erythroderma is that the scaling is fine and branlike. In this case the scales are large and adherent.

ULCUS DURUM (?). Presented by DR. ADOLPH ROSTENBERG.

A woman, aged 20, an American, married, had had the condition for three months. She had had a miscarriage about two years prior to presentation. She had a baby 3 months old. A prenatal Wassermann test made during her last

pregnancy was negative. There was no history of syphilis. The condition had started three months prior to presentation. In September she was seen at the clinic for diseases of the eye of the Sydenham Hospital where the condition was diagnosed as multiple chalazia. As the patient did not improve under treatment, a Wassermann test was made and found to be 4 plus; the Kahn test was also found to be 4 plus. She was then transferred to the department for diseases of the skin a few days prior to presentation, and a futile search was made for spirochetes.

An indurated tumor was found over the entire lower eyelid; on either side there were two large pinhead-sized excoriations. There was no preauricular or postauricular adenopathy. There was no evidence of any secondary lesions either on the skin or on the mucous membranes.

DISCUSSION

DR. HERMAN GOODMAN: From the clinical aspect, the lesion is that of primary syphilis. It is sharply demarcated and indurated, and there is no acute inflammation. The absence of spirochetes and the long duration are indications against such a diagnosis. The first factor can be explained by the preliminary treatment and the fact that only one examination was made. The duration is not so easily explained, but chancre may have been superimposed on a nonsyphilitic lesion which preceded it. It is presumed that the patient had a negative Wassermann reaction at the time her child was born. A 4 plus Wassermann reaction at this time indicates a recent infection.

DR. ISIDORE ROSEN: I regard this case as one of primary syphilitic lesion of the eyelid. The marked induration and the cleancut character of the ulceration, its persistence and its failure to respond to local therapy are strong indications in favor of that diagnosis.

DR. JOSIAH THORNLEY: The location of the lesion, the duration of three months, without much improvement or change, makes me inclined to doubt the fact that it is a primary lesion. I saw a young woman, with a 4 plus Wassermann reaction, who had a similar lesion on the cheek; she was treated for impetigo. In neither condition was there glandular involvement. She recovered promptly under antisyphilitic treatment. I think that this is an unusual manifestation of either secondary or tertiary syphilis, as the evidence is hardly sufficient for one to make a definite diagnosis of a primary lesion.

LUPUS ERYTHEMATOSUS (?). Presented by DR. PAUL GROSS.

In J. A., a man, aged 20, born of Syrian parents, whose familial and past histories were unimportant, the first lesions had developed on the forehead one year prior to presentation, and four months prior to presentation the condition on the upper lip had appeared. There were two lesions the size of a quarter on the forehead and a dime-sized patch on the right side of the upper lip. The lesions were annular and slightly elevated. The periphery was darker than the center. There were slight atrophy in the central portions of the lesions and evidences of follicular plugs in the lesions. Study of the sections taken for biopsy definitely excluded a diagnosis of sarcoid. The diagnosis was "probably lupus erythematosus." Roentgenograms of the hands showed the bones to be normal.

DISCUSSION

DR. ISIDORE ROSEN: I suggest the diagnosis either of granuloma annulare or of lichen planus annularis. The unusual configuration and color tend to rule out the diagnosis of lupus erythematosus in this case. I think that the violaceous hue, the small annular lesions, some having slightly elevated edges, and the absence of all follicular involvement or scaling are factors in favor of the diagnosis of granuloma annulare or of lichen planus annularis.

DR. GEORGE B. ANDREWS: My impression was similar to that of Dr. Rosen, namely, that this patient has lichen planus.

DR. EUGENE TRAUB: I, too, received the impression of lichen planus from the annular appearance of the lesions, with borders that are definitely elevated (papular), which is the important differentiating feature.

DR. PAUL GROSS: The diagnosis was influenced by the histologic report. Clinically, we considered sarcoid of Boeck, lupus erythematosus and lichen planus. The lesions have changed under therapy with gold compounds.

ERYTHEMA FIGURATUM PERSTANS. Presented by DR. EUGENE TRAUB.

D. G., a youth, aged 16, born in the United States, a student, stated that his present trouble had begun six months before his first visit to the Stuyvesant Square Hospital, on May 18, 1932. He presented circinate and serpiginous lesions of various sizes. There were a few lesions that suggested an iris type, and the borders consisted of urticarial-like papules that in places made segments of a circle. The lesions enlarged slowly by peripheral extension, leaving a pigmented center. This enlargement was so gradual as to be hardly noted from one visit to the next.

The past history was irrelevant except for marked chronic constipation. The patient had undergone a tonsillectomy at the age of 4. Roentgen examination of the teeth gave negative results, except for caries in a lower molar and bicuspid. Examination of the nose and throat was negative except for mild chronic rhinitis. The genito-urinary examination gave negative results.

Urinalysis performed as a routine measure gave negative results as did examination of the urine for lead. Examination of the urine for arsenic, however, showed: specific gravity, 1.025; solids, 4.5; 0.021 mg. of arsenic per hundred grams of solid. The Wassermann reaction was negative. Chemical examination of the blood gave negative results.

The case appeared to be one of primary tooth or gingival infection with a tremendous secondary implant of streptococci in the intestinal tract. Treatment consisted of calamine lotion applied locally, baths of sodium bicarbonate, saline purgatives and high colonic irrigations; autohemotherapy, together with a series of twelve injections of vaccine, prepared by Dr. Burbank, was also employed. The patient was placed on a diet low in carbohydrates.

DISCUSSION

DR. FRED WISE: The clinical appearance certainly coincides with the description of the various conditions described under that name. The chronicity, the persistence of the lesions in a single area, the lack of change over long periods of time, the appearance of the papules in general, the circinate elements and the tendency toward a sloping of the inner border of the lesions (originally described by Darier) are all points in favor of the diagnosis.

DR. ADOLPH ROSTENBERG: I believe that although there are rather too many small papular lesions and the margin of the more typical lesions is more infiltrated than in the ordinary case, the condition is characteristic for Darier's "erythema annulare centrifuge."

DR. FRANK C. COMBES, JR.: This patient presents the condition originally described by Darier as érythème annulaire centrifuge and later by Colcott Fox as erythema figuratum perstans. Darier later expressed preference for the term érythème papulo-circiné migrateur since the initial lesion is not an erythema but a raised papule.

DR. EUGENE TRAUB: A discussion as to terminology is always very interesting, but we have been particularly engaged in this case in working up the etiology. The patient was thoroughly examined for foci of infection in the teeth, tonsils, sinuses and gastro-intestinal and genito-urinary tracts. The tonsils had been removed at the age of 4, but some infected remnants were still present. There was

a mild chronic rhinitis; otherwise the examination of the nose and throat gave negative results. The dental and genito-urinary examinations gave entirely negative results. The results of the examination of the urine, including the test for lead, the Wassermann test and the results of chemical examination of the blood were normal; 0.21 mg. of arsenic per hundred grams of solid was found in the urine. The complement-fixation test on the blood as performed by Dr. Burbank was the most interesting part of the examination, and a vaccine prepared on the basis of his findings caused the first improvement in the symptoms. Dr. Wende, who described a number of cases under this particular title in 1905, attached much significance to a condition of the gastro-intestinal tract as a causative factor in some of the cases. At the present time, the eruption is regressing so slowly that any further therapeutic suggestions would have been welcome.

A Case for Diagnosis (Lymphogranuloma Inguinale ?). Presented by Dr. David Bloom.

Z. A., a man, aged 45, Polish, a laborer, presented enlarged cervical and submaxillary glands on the left side of the neck. The anterior third of the tongue was cherry red on the upper surface, granular and firm.

Five months prior to presentation, following sexual relation with a Negress, a "pimple" developed on the tip of the tongue, to the right of the midline, which the patient cut with a razor blade two weeks later. Soon afterward, the whole anterior part of the tongue became red and swollen, and two weeks later the whole left side of the neck became markedly swollen and tender.

Several incisions were made which yielded pus.

Biopsy of the lesion of the tongue did not show a specific pathologic process. A Frei test made by Dr. Curth of the Presbyterian Hospital was positive on two occasions. The patient did not give a history of a previous penile lesion with involvement of the glands. The Wassermann test was negative.

DISCUSSION

Dr. Curth (Vanderbilt Clinic): This patient was first treated for syphilis by a private physician. He did not respond to treatment and was sent to Dr. Kaufmann. We considered a number of possible diagnoses: (1) Hodgkin's disease, (2) tuberculosis or (3) syphilis without response to treatment. When I first saw the patient and heard the history, I remembered having seen a similar case at Buschke's Clinic, Berlin, which I reported in the *Klinische Wochenschrift* (no. 37, p. 1709, 1931). I did the Frei test in this case, and it was positive. I took pus from the glands of the neck and inoculated this pus into other patients with lymphogranuloma inguinale, and these patients gave positive reactions. Biopsy of the section from the tongue showed only a chronic inflammatory condition. Biopsy of a section from the neck gland was not much of a success. I think that the case is the second one of extragenital lymphogranuloma inguinale starting from the tongue that has been recorded.

Dr. Marion Sulzberger: What name would the members like to give this disease? I am sure that the condition seen in this case is called lymphogranuloma inguinale when it occurs in the inguinal region, but it seems rather absurd to call it by this name when it occurs in the mouth, in the submandibular region, in the axilla and in the rectum. This is one of the reasons why Dr. Wolf and I suggested the name "lymphopathia venerea," which covers all the manifestations of the disease (*Brit. J. Dermat.* **44**:192 [April] 1932; *J. A. M. A.* **99**:1407 [Oct. 27] 1932).

I think that the diagnosis must be considered as proved in view of the crossed Frei test, antigen from other patients producing a positive reaction in this patient and antigen from this patient producing a positive reaction in patients known to have lymphogranuloma inguinale. The question of nomenclature is important. Some cases of axillary involvement have been recorded, and we know that especially in women there is frequently no inguinal involvement, but that only the

rectal or the perirectal region or the vulva may be affected. Many cases of stricture of unknown origin are undoubtedly due to this disease.

DR. W. CURTH: When we first saw the patient he presented very superficial chancre-like lesions on the tongue. The eruption is now a diffuse glossitis. I do not understand why this extensive glossitis is present. I hear from Professor Buschke that the other patient, who was seen in Berlin, showed an extensive glossitis of long duration.

DR. E. WILLIAM ABRAMOWITZ: It is known that the primary lesion of lymphogranuloma inguinale is so mild that it may be missed. In this case, the primary lesion is said to have started on the tongue, and yet the tongue is still of abnormal contour. Nevertheless, I agree with the diagnosis, although it is possible that there is some other factor which prevents the tissues of the tongue from healing completely.

DR. MAX SCHEER: I think that the lesion on the tongue is comparable to the lesion observed on the female genitalia (esthiomène) or the anorectal syphiloma (so-called) which may be found in both sexes in this disease.

DR. MARION SULZBERGER: I think that the type of lesion now seen in this tongue must be interpreted as Dr. Scheer says, namely, as an inflammatory process of the mucous membranes after infection with the virus of lymphogranuloma inguinale. The diffuse sclerosing is not the primary lesion but an extension of a primary lesion through the lymphatics. It seems that the primary lesion of lymphopathia venerea remains as a circumscribed small chancre only in the skin. As soon as it gets into the deeper tissues the process becomes diffuse, following the small lymphatics and causing cicatrization and eventually retraction. This is the process which one sees in this tongue and which one finds so frequently perirectally, where it eventually causes the strictures, which were formerly such puzzles to us.

DR. DAVID BLOOM: If the condition is lymphogranuloma inguinale — and it probably is — it is a very unusual case. Hellerström (*Acta dermat. venereol.*, supp. 1, p. 105, 1929) cited two cases of lymphogranuloma inguinale of the axillary glands, one reported by Klotz the other by Favre, both in surgeons who have operated on inguinale buboes. Hellerström himself reported a third case, quite similar to the former two cases, in a physician who had a positive Frei test twenty-three years after the infection. Buschke and Curth (*Klin. Wchnschr.* **10**:1709 [Sept. 12] 1931) reported a case which is very similar to the one presented tonight. This is the fifth case of extragenital localization and the second case in which the primary infection involved the tongue. The persistence of the lesions on the tongue was plausibly explained by Dr. Sulzberger but the injury produced by the razor may have caused it.

EPIDERMOLYSIS BULLOSA ACQUISITA (?). Presented by DR. MARION SULZBERGER.

A. T., from the dermatologic clinic of the Post-Graduate Hospital had had the condition for six months. The lesions were located on the dorsal surfaces of the hands, and the helices of the ears presented spontaneous bullous lesions appearing on normal skin. There was a positive Nikolsky sign of the hands. The patient's general health had been good. The blood count was reported as normal. The potassium iodide test was negative. The mucous membranes had never been affected. Biopsy observations were suggestive of dermatitis venenata.

DISCUSSION

DR. GEORGE B. ANDREWS: I agree with the diagnosis of the presenter. Clinically, the condition is very rare. I think that this case should be studied carefully in order for one to make up one's mind fully about the diagnosis, but it fits in with my clinical conception of this disease.

DR. CHARLES WOLF: This patient has been a seaman for practically twenty years. I asked him whether he had been exposed to the sun during his trips on the high seas. He stated that at times on certain trips he had been exposed to the sun. I wonder whether a diagnosis of bullous erythema solare would be in order? These bullous lesions appear spontaneously. I believe that the patient is still getting these lesions because of sun rays acting on the tissues after prolonged exposure.

DR. MARION B. SULZBERGER: I put down the diagnosis of epidermolysis bullosa "acquisita" (which it would be better to call "tarda") with a question mark after it and mentioned several other differential diagnostic possibilities: (1) hydroa vacciniforme, (2) localized pemphigus and (3) erythema multiforme. Each of the other diagnoses has certain grave factors against it. Almost by elimination we have come to the conclusion that the condition is epidermolysis bullosa tarda. Dr. Wolf's theory hardly seems logical to me. In this patient bullae continue to appear for weeks and months after cessation of exposure to the sun. We know that in epidermolysis bullosa it is not possible to get a history of trauma at the site in which certain of the bullous lesions appear. They may therefore seem to appear spontaneously. In this case a lesion appears at the site over which the skin is rubbed, but only when this is done on the hands. This is an observation which favors the diagnosis.

The lesion which can be caused experimentally in this case is not a bulla but rather a dehiscence of the superficial layers similar to the Nikolsky sign, except that the removal of the epidermis here leaves a rather moist area veneati; I have noted this in several cases of epidermolysis bullosa, and believe that the Nikolsky sign in pemphigus is rather dryer in type than that which is found in this case.

ERYTHROPLASIA OF QUERYAT. Presented by DR. MARION SULZBERGER.

The patient from the clinic for diseases of the skin of the Post-Graduate Hospital was previously presented before the section on Oct. 4, 1932, as having a case for diagnosis; the diagnosis of precancerosis or drug eruption was suggested. The patient had resisted all ordinary therapy up to that time. Since presentation the patient had received about 5 units of roentgen rays (1,250 roentgens), some filtered (through 3 mm. of aluminum) and some unfiltered.

DISCUSSION

DR. FRED WISE: This patient was previously presented under the mistaken diagnosis of granuloma inguinale. Subsequently, at the suggestion of Dr. Goldenberg, a diagnosis of erythroplasie de Queryat was made, and the histologic sections confirmed the diagnosis of this so-called precancerosis. The patient was again presented for suggestions as to therapy.

DR. E. WILLIAM ABRAMOWITZ: I suggest that the lesion on the penis should be removed by electrodesiccation, as I have read of some good results obtained with this method of treatment. Petes reported three cases in which the patients were treated with diathermocoagulation (*Bull. Soc. franç. de dermat. et syph.* **38**:877, 1931).

DR. MAX SCHEER: I saw this patient when he first came to the clinic and have examined him frequently since then. At the time of his first visit I was unaware of the existence of the disease known as erythroplasia of Queryat and made a diagnosis of a superficial epithelioma or a possible drug eruption. We ruled out drug eruption. Later, some one familiar with tropical diseases found the organisms of granuloma inguinale, and on the strength of this observation I presented the patient at the Manhattan Dermatological Society. However, the slides were examined by Professor Jadassohn who demonstrated that the so-called organisms were but granules of eosinophil leukocytes.

When I looked up the literature (most of which seems to be in French), it was evident that this case corresponds closely to the condition described by Queryat.

In spite of roentgen treatment, the patient's condition is worse. The original three or four isolated lesions have coalesced and involve nearly the entire glans. I think that the lesion should be destroyed by surgical diathermy.

DR. MARION SULZBERGER: I am showing this patient again because at the last meeting I promised I would report on the findings and progress. When the patient was first presented before this section, I labeled the condition as a case for diagnosis: precancerosis or drug eruption? I think that one can now say with certainty that it is a precancerosis, malignancy threatening. All the European physicians to whom I showed these sections now agree that the condition is histologically a precancerosis of the type known as erythroplasia. I present the case tonight with the established diagnosis and should like suggestions as to therapy. I am indebted to Dr. Goldenberg for first calling my attention to the resemblance of this case to Queryat's erythroplasia.

LICHEN PLANUS LINEARIS (?). Presented by DR. LOUIS TULIPAN.

In P. S., a Negro boy, aged 6, a small lesion appeared on the right ankle four years prior to presentation. The remainder of the eruption had been present for nine months. On the right lower extremity, from the buttock to the lateral malleolus, there was a band of small, pinhead-sized, shiny, flat papules lighter in color than the normally brown skin. Many confluent patches were also present. There were many similar papules elsewhere on the body, some in linear formation. There were also, especially on the arms, depigmented superficial scars.

DISCUSSION

DR. ISIDORE ROSEN: I suggest the possibility of lichen nitidus. The pinhead-sized grayish-white lesions without central umbilication, as well as the complete absence of color, are indications against the diagnosis of lichen planus. In my opinion, the presence of linear lesions does not make this case one of lichen planus, for there are other diseases which develop in scratch marks. The way to decide definitely would be to make a histologic examination.

DR. OSCAR LEVIN: The patient showed innumerable papules ranging in size from that of a pinhead to that of a grape-seed. Some showed a tendency toward grouping, and in places there was linear formation. Lichen planus was suggested only by the occasional shimmer and the linear grouping. I cannot agree with the diagnosis of lichen nitidus. Closer examination of the skin revealed that the lesions consisted of small papules, many of which showed central follicular umbilication and larger conical papules with scaling, and the largest ones showed central necrosis and crusting. I would diagnose the case as one of lichenoid tuberculosis (lichen scrofulosorum).

DR. LOUIS TULIPAN: It is difficult to associate the linear lesions of the leg with the lesions on the body. There are no typical lichen planus lesions in the linear dermatosis of the leg, while the papules on the back and chest, in linear formation, present a picture often seen in lichen planus. In addition, lesions in the skin of a Negro are not quite so typical as those in the skin of a white person. In lichen scrofulosorum, such lesions usually clear up after a short while and would not last four years without change. The most likely diagnosis is that of lichen planus.

SYPHILIS OR LEPROSY. Presented by DR. LOUIS TULIPAN.

J. S., a man, aged 31, an engineer, had had an eruption for five years. The patient stated that he had not had a chancre. He had never been outside of the United States.

On the chest, abdomen and back were lesions that ranged in size from that of a dime to that of a silver dollar and larger. The color was violaceous. The borders were nodular. The center of the lesion was flat and smooth. There were a few infiltrated, violaceous, flat, ovoid lesions covered by scales. The eruption was bilateral. There were no scars. A few enlarged lymphatic glands were noted. An Argyll Robertson pupil was demonstrated. A blood count was normal. A microprecipitation test was strongly positive (Rosenthal). The Wassermann reaction was 4 plus. A section had been taken for biopsy.

DISCUSSION

DR. ANDREW GILMOUR: I think that clinically the condition is leprosy.

DR. FRED WISE: The only suggestion I would make is that the word "tuberculoid" leprosy should be used, so as not to confuse one and make one think of the possibility of tuberculosis. Tuberculoid leprosy of Jadassohn indicates a histologic structure like tuberculosis in leprosy lesions of the skin.

DR. J. FRANK FRASER: From the appearance of the lesions I would not venture an opinion as to whether this condition is leprosy or syphilis. Is any anesthesia or paresthesia present? So far as finding bacilli is concerned, I have never had any difficulty in demonstrating Hansen's bacillus in cases of nodular leprosy. In the maculo-anesthetic type, demonstration of the organisms is more difficult.

DR. HERMAN GOODMAN: My clinical interpretation of the nodular, disseminated multicircular lesions is that the patient has mycosis fungoides. The color is not that of mycosis fungoides. There is no history of preceding pruritic lesions, although this is not essential to the diagnosis. The nasal discharge should be examined for leprosy bacilli after a dose of potassium iodide has been given.

DR. SIGMUND POLLITZER: I hesitate to express an opinion about this case. I am not at all satisfied that the condition is leprosy; on the contrary, I rather think that it is not. The clinical features are against mycosis fungoides, sarcoid, syphilis and leprosy. I think that a diagnosis of the benign form of pemphigus vegetans should be seriously considered. Against the diagnosis of leprosy is the fact that the patient was born in New York and has never been in a country where there are lepers. This circumstance, of course, is not final, but has a very great weight.

Regarding the histologic picture, I cannot agree that this is the picture of leprosy. The striking and characteristic feature of a nonulcerated leproma is lacking; the infiltration extends up to and into the epidermis, while in a leproma there is always a line of condensed connective tissue separating the infiltration from the epidermis.

DR. J. GARDNER HOPKINS: It seems to me that the case does not resemble any case of leprosy I have seen or any picture I have seen. I have never seen nodular lesions that occurred in serpiginous plaques, clearing in the center. I have not had enough clinical experience with the disease to make sure that this does not occur. Clinically, the condition looks more like syphilis or a case of sarcoid. From the histologic observations, I am not sure that one can differentiate tuberculoid granulomas. Sarcoid, leprosy and some forms of syphilis can present quite indistinguishable histologic pictures.

DR. HERMANN FEIT: Dr. Wade of the Philippine Islands, who studied lepra conditions in all parts of the world, particularly from a pathologic standpoint, told me that nodular syphilis and tuberculoid leprosy could not be distinguished microscopically. The patient does not show any evidence of enlargement of the nerves or anesthesia so far as I learned. The Wassermann test is often positive in leprosy.

DR. ISIDORE ROSEN: The clinical features are indications in favor of the diagnosis of leprosy, rather than of syphilis: for example, the color, the glossy appearance, the smooth, velvety feel of the skin and the persistence of the lesions

without any tendency to break down or heal spontaneously. I think that the histologic observations also substantiate this diagnosis.

DR. GEORGE C. ANDREWS: I am inclined to make a diagnosis of sarcoid. That is my clinical impression.

DR. J. AMBLER, Cleveland (by invitation): With a 4 plus Wassermann reaction of the blood and suggestive clinical signs of involvement of the central nervous system, namely, the fact that the patient was picked up in an unconscious condition on the street a week ago, the presence of a typical Argyll Robertson pupil makes the diagnosis of syphilis most likely.

DR. OSCAR LEVIN: When I first saw the patient, two diagnoses were suggested: mycosis fungoides and syphilis. However, the absence of itching and scaling and the smooth character of the surface of the lesions suggest a diagnosis of syphilis rather than that of mycosis fungoides. The lesions also looked somewhat translucent. They were dark brown, with a yellowish tinge. The surface looked smooth and glossy, and on palpation the lesions felt soft and doughy. Other diagnoses therefore considered were those of sarcoid and leprosy. The clinical appearance suggested leprosy, and examination of the tissue on a slide under the microscope showed large spaces or cells that looked mucoid and suggested the appearance of lepra cells. If the condition is leprosy, the bacilli should be found easily. I favor the diagnosis of leprosy.

DR. FRANK C. COMBES, JR.: Dr. Pollitzer and I examined the pupils closely. They react to light rather sluggishly. They are not, strictly speaking, Argyll Robertson in type.

DR. SAMUEL PECK: The characteristic histologic feature in this case, the large foamy type of cell, plays an important rôle in a number of diseases of the skin. It is often seen in mycosis fungoides, leprosy and granuloma inguinale. It must be borne in mind that this type of cell reaction can predominate in drug eruptions. This was well exemplified in Dr. Eller's fatal case of iododerma.

If these types of cells are examined for fat, it is not found. The foamy appearance is due to a mucoid-like substance. The histologic appearance is not due to the dissolving out of fat by fixation as in the case of xanthoma. The histologic picture is more characteristic of leprosy than of syphilis.

DR. PAUL BECHET: I am inclined to agree with those who favor the diagnosis of leprosy. I think that they have the best of the argument. I am opposed to the use of the word tubercular in connection with either leprosy or syphilis. It should be confined entirely to the description of actual tuberculosis of the skin. To my mind, nodular leprosy and nodular syphiloderm are terms much less confusing and more descriptive of actual facts. The matter is not of much importance to the dermatologist, but it must be confusing to others, and, for that reason alone, the word tubercular should be dropped in describing diseases of the skin which are nontuberculous in character.

DR. LOUIS TULIPAN: The differences of opinion expressed tonight recall those offered when the case was first seen a few days ago, namely, syphilis, lepra, tuberculosis, leukemids or mycosis fungoides. As to lepra, the patient has never been outside of the Atlantic seaboard. When a drug eruption was considered, there was a firm denial of the taking of any drugs. A blood count was normal; a microprecipitation test (Rosenthal) was strongly positive, and a Wassermann reaction of the blood was 4 plus. A microscopic section did not show the typical changes of syphilis or those of lepra.

ERYTHEMA MULTIFORME OR DRUG ERUPTION (?). Presented by DR. SAMUEL FELDMAN.

N. M., aged 34, a housewife, entered the Morrisania Hospital on Sept. 14, 1932, suffering from bullous lesions on the lips, in the mouth and on the extremities. She complained of a burning sensation in the mouth, and stated that outside

of occasional remissions, the condition had persisted for about three years. She had been in good general health.

There were a large bleb on the upper lip and several on the vermilion border of the lower lip, the under surface of the tongue, the cheeks and on the hands and feet. In the mouth, the bullae were macerated and emitted a foul odor, whereas on the skin the blebs were clear and odorless.

The patient had been instructed to use a solution of sodium perborate as a mouth wash, and the lesions in the mouth and on the lips began to heal. Improvement continued until September 20, when three large bullae appeared on the arms. The content of these blebs was turbid, and one of them was surrounded by an inflammatory zone. The patient had previously stated that she had not taken any drugs, but on this occasion she admitted having taken stanoxyl several days prior to the appearance of the new bullae. The stanoxyl was discontinued, and since then there had been a constant improvement in the lesions. On October 3, the patient was ordered to resume the ingestion of the drug for the purpose of testing the patient's sensitivity to it.

Examination of the urine gave normal results, both chemically and microscopically. The blood count and the differential count were normal. Chemical examination of the blood gave values within normal limits. The Wassermann test was negative. A patch test was made with 33 per cent potassium iodide ointment, with the result that a crop of acne-like pustules developed in the tested area.

Cultures made from the contents of the bullae were negative.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: In addition to the eruption that this patient presents, which is attributed to tin by Dr. Feldman, I was struck with the yellowish tinge of the patient's skin, particularly on the palms. As she has been on a vegetable diet for the past six months, it seems to me that she also has a mild case of carotinemia.

SARCOMA KAPOSI (?). Presented by DR. SAMUEL FELDMAN.

H. L., a chauffeur, aged 32, contracted syphilis in 1931. On the roof of the mouth, at about the center of the hard palate, there was a lozenge-shaped area about a half an inch long and one-fourth inch wide, situated anteriorly. The patch was raised only slightly above the surface of the mucous membrane of the palate; it was smooth but firm to the touch, and was bluish red. At the anterior end of the plaque, there was a small protuberance from 3 to 4 mm. in thickness. It was grayish and firm. This nodule was removed early in May, 1932, after the patient had received a sufficient amount of antisyphilitic treatment. The wound healed promptly, and there were no changes in the remaining lesion until September, 1932, when a new nodule appeared close to the biopsy wound.

Histologic study showed that there was a great increase in the number and size of the blood vessels with hemorrhages into the adjacent tissue. There was an increase in fibrous tissue. In some areas the cellular element predominated. The cells were oblong or spindle-shaped and were packed close to one another.

DISCUSSION

DR. SIGMUND POLLITZER: I do not think that this growth is sarcoma. That disease begins almost invariably on the lower extremities. To make a diagnosis of Kaposi sarcoma from a single lesion on the palate is unsafe. I have read reports of histologic examinations in that disease for forty years. There is so much discrepancy in the views as to what the Kaposi sarcoma really is that I do not feel like making that diagnosis from a histologic section. It is possible that this is a case of that disease, but that is as far as I should like to go.

DR. ISIDORE ROSEN: The diagnosis of Kaposi's sarcoma is an excellent suggestion, for I have seen patients with this disease who present lesions of the

hard palate and other portions of the oral cavity. The occurrence of an associated papillomatous lesion would also tend to corroborate the diagnosis, because occasionally papillomatous lesions of the feet are seen in cases of Kaposi's sarcoma.

DR. EUGENE TRAUB: From the clinical appearance of the lesion this evening and the history of recurrence following removal (inadequate) and since the histologic examination does not definitely exclude the possibility, I believe that the diagnosis of epulis, used in its broadest sense, is the best classification of this tumor.

DR. J. FRANK FRASER: Have any of the members observed lesions of Kaposi's sarcoma confined to the mucous membranes of the mouth?

DR. SIGMUND POLLITZER: So far as I know, a single lesion confined to the mucous membrane of the mouth has never been observed in the multiple hemorrhagic sarcomatosis of Kaposi.

DR. LOUIS CHARGIN: There is no question but that Kaposi's sarcoma is occasionally observed on the mucous membranes of the mouth. It is usually seen in association with lesions elsewhere on the body. Although the initial lesions in Kaposi's sarcoma are usually seen on the extremities, the disease does occasionally begin elsewhere on the body. For instance, in the literature there are numerous records of cases in which the first lesions were observed on the ears, and there seems to be no reason why it may not take origin in the mouth as well. The pathologic process in this case, namely, an angiosarcoma, may very well fit into the picture of Kaposi's sarcoma. The process has existed for a long period of time without showing a tendency to spread. This is a point against sarcoma. In view of the fact that the clinical aspect is that seen in Kaposi's sarcoma, this is suggested as a possible diagnosis in this case.

DR. J. GARDNER HOPKINS: There is a common type of benign tumor having the structure of angioma which occurs on the gums and is known as a fibrous epulis. It seems possible that similar tumors might occur on the hard palate.

DR. SAMUEL FELDMAN: Before Dr. Feit left he said that he had observed a patient with Kaposi's sarcoma in the mouth. The patient had an injury of the foot later, and typical Kaposi sarcoma developed on the foot afterward.

Kaposi's sarcoma suggests itself because of the long duration of the disease. I saw the patient last summer. He came in with secondary syphilis. There was no chance to perform biopsy at that time, and it took a long time to get the syphilis under control. The new nodule is not a recurrence of the excised lesion. It sprang up at some distance from the scar.

DR. J. FRANK FRASER: I think the presenter should submit a series of slides to a committee, say three pathologists who will examine them and report at the next meeting of the Section. I suggest Drs. Pollitzer, Hopkins and Satenstein.

GRANULOMA: POSSIBLY DUE TO FUNGOUS INFECTION. Presented by DR. DAVID BLOOM.

T. F., aged 38, an American Jewess, presented on the dorsum of the right hand, outer and inner aspect of the right ankle, and outer aspect of the left ankle, irregularly shaped ulcerations with undermined soft edges from under which pus was oozing and which could be easily expressed. Some of the base was covered with granulation tissue and some with strips of skin from under which pus could be expressed.

The condition had begun with swelling accompanied by mild pain; the lesions were incised two weeks later, and they had been draining pus since. Under wet antiseptic dressings the condition of the skin improved in the center, but progressed peripherally.

Urinalysis showed a trace of albumin and some leukocytes. The blood count revealed marked anemia, there being 2,160,000 red blood cells, with a hemoglobin of 45 per cent, and 7,800 white blood cells, 74 per cent polymorponuclears and 26 per cent lymphocytes. The chemical composition of the blood was normal.

The Wassermann test of the blood was negative. The blood culture did not show any bacterial growth. The feces showed in culture a Gram bacillus (coli) and contained blood due to numerous ulcerations in the rectum and sigmoid. Pus showed in culture a growth of Staphylococcus aureus. Fungus examination was negative microscopically, and a culture tube seeded one week previous to presentation was still negative for fungi. Amebae were looked for in the feces, pus and ulcers of the rectum, but were not found.

Proctoscopic examination revealed ulcerative coloproctitis and ulcerated internal hemorrhoids.

Roentgenographic examination of the lungs was negative. Roentgenographic examination of the feet revealed a marked degree of atrophy of all the bones. The right hand showed besides the same marked atrophy of the bones also a marked periosteal reaction along the shafts of the fourth and fifth metatarsals.

Biopsy performed on the affected skin showed a fairly regular acanthotic epidermis. In the cutis the predominating feature was granulation tissue in all stages of development. In the cell infiltration, plasma cells predominated. There was no tubercle formation. In one of the specimens examined a double contoured body (either Blastomyces or Coccidioides) was found. There were a fairly large number of well developed giant cells. Tissues from the hand and leg were similar.

DISCUSSION

DR. J. GARDNER HOPKINS: The lesions on the hands and feet did not look like granuloma; they look more like trophic ulcers. I think the symmetry of the lesions on the feet and one hand suggests some trophic disturbance. I should like to know more about the case and study the sections carefully.

DR. SIGMUND POLLITZER: The slide is a picture of a granuloma. The one cell that suggested a possible coccidioidal organism is certainly not truly a double-contoured cell; it is a cell with degeneration of the cell membrane.

DR. MAX SCHEER: The marked anemia and ulcerations on the ankle suggest the possibility of a sickle cell anemia, a condition quite rare in the white race. I would suggest examination of a blood smear for sickle-shaped red cells.

DR. DAVID BLOOM: In addition to the data given in the history, I wish to add that the patient was, when I saw her two months ago, in a moribund condition, and when I was told that the bacteriologic examination revealed only staphylococci, my provisional diagnosis was staphylococcic infection of the skin due to a general low resistance. And, in fact, the supportive treatment as advised by me, which consisted of several transfusions, i. e., liver extract, etc., had quite a marked effect on the lesions. Potassium iodide was also given to the patient at the suggestion of Dr. Abramowitz, and was of marked influence.

DR. LOUIS TULIPAN: I suggest that Dr. Bloom try inoculations into mice or guinea-pigs if coccidioidal bodies are found.

DR. E. WILLIAM ABRAMOWITZ: I suggested the possibility of a granuloma due to some yeastlike organism, owing to the clinical appearance of the lesions. There were sharply limited patches involving the ankles and right hand, showing a definite border that embraced various ulcerated areas and cutaneous abscesses. There was comparatively little pain and no temperature to speak of. The patient was quite anemic, but the blood picture showed nothing abnormal except a drop in the red cell count and in the hemoglobin. The laboratory findings were of no help, excepting that tuberculosis and syphilis were excluded. The patient has shown almost a 25 per cent improvement in the last few days on administration of mild doses of potassium iodide. I intend to have studies made and will report at the next meeting.

NEVUS PIGMENTOSUS: OUTBREAK OF INNUMERABLE LESIONS FOLLOWING EXCISION OF A LARGE SINGLE LESION. Presented by DR. PAUL BECHET.

A girl, aged 9, had had since birth a large hairy nevus over the right temple which measured about 6 mm. in diameter. She had at the time a few satellite

lesions. At the age of 2, the large nevus was excised in a Detroit Hospital, and was covered with a skin graft.

At the time of examination seven years later, the site of the nevus showed a smooth pliable scar, but on the face and all over the body were several hundred various sized, pigmented lesions, many of which were hard and nodular, with here and there distinct inflammatory changes. The child seemed to be in good health and had not lost any weight.

CONGENITAL TELANGIECTASIA. Presented by DR. SAMUEL PECK.

The skin on the trunk presented a peculiar bluish appearance like an exaggerated cutis marmorata. The left side was more affected than the right. On closer examination there was seen marked dilatation of the superficial blood vessels and the appearance of a secondary circulation like that seen in obstructive liver disease or heart failure. The vessels which were seen varied from small telangiectases to those as large as a pencil. Over the buttocks it resembled a flat hemangioma. The extensor surfaces of the arms showed similar prominent vessels up to the finger-tips. The finger-tips themselves showed small dilated vessels. The process stopped above the inguinal region on the right side, and on the left side it extended to the middle of the thigh. On lying down or on stroking of the skin, the vessels could be emptied to a certain extent. The mucous membranes were free.

General physical examination, with the exception of a slight bulging of the left side of the chest and unusual enlargement of the hands and feet, gave negative results. The blood count was normal, as was the blood smear. The Wassermann reaction was negative. The Pirquet reaction in 1929 was negative.

BISMUTH PIGMENTATION ON BUCCAL MUCOSA. Presented by DR. LOUIS CHARGIN.

The patient had had a syphilitic eruption of six months' duration and had up to the time of presentation received twelve injections of arsphenamine and seventeen of bismuth. The mouth hygiene was found to be very poor. The patient presented a marked bismuth line along the teeth-gum margins and pigmentation, especially marked on the mucous membranes of the left cheek, which had been present for several days.

PIGMENTATION FOLLOWING LUPUS ERYTHEMATOSUS (?). Presented by DR. HERMAN SHARLIT.

B. C., a girl, aged 13, had had the condition for three months. She presented over the lower half of the forehead, both malar eminences and upper lip, a reticulated, light brown pigmentation with a very fine telangiectasia, dispersed throughout the pigmentation. There was a suggestion of a slight atrophy within the mottling.

The patient gave a history that three months previous to the appearance of the pigmentation an erythematous rash which looked like a sunburn had developed. During the course of the summer the erythema disappeared, and the pigmentation appeared. One year previously a similar rash had appeared on the upper lip and had left a pigmented patch. About two weeks before admission to the clinic at Bellevue Hospital, there had developed pinhead to pea-sized, infiltrated, erythematous, itching, prurigo-like papules on the backs of the hands and the extensor surface of the upper extremities.

Biopsy confirmed the diagnosis of lupus erythematosus.

HERPES ZOSTER (GANGRENOUS) WITH VARICELLIFORM ERUPTION. Presented by DR. HERMAN SHARLIT.

In a man, aged 43, an eruption had developed on the left breast eleven days prior to presentation. Several days later he noticed "pimples" over the rest of

the trunk. He had a cold the first day of his initial eruption and took "bromo-quinine." He presented groups of bullae and vesicles on an erythematous base over the left breast, axillae and arm. There were papules and vesicles containing turbid fluid, found scattered over the trunk. Some of the herpetic lesions were now gangrenous.

PITTSBURGH DERMATOLOGICAL SOCIETY

FREDERICK AMSHEL, M.D., *Secretary*

Regular Meeting, Oct. 20, 1932

CLAUDE B. NORRIS, M.D., *President, in the Chair*

PEMPHIGUS. Presented by DR. GEORGE J. BUSMAN.

A. K., a woman, aged 30, married, a housewife, presented maceration of the surface of the pharyngeal, buccal and nasal mucous membranes. The lesions were those of bullae that had apparently ruptured, leaving raw, denuded areas and areas covered with a white, spongy pellicle. There was some involvement of the gums. The inner canthus of each eye was injected, particularly the region of the lacrimal sac. There were no lesions on the trunk or extremities. The Wassermann test of the blood was negative, as were smears and cultures for Vincent's angina. The condition was of from one to two months' duration. No history of the ingestion of drugs, metals or other substances was obtained.

DISCUSSION

DR. LESTER HOLLANDER: I favor the diagnosis of pemphigus. I advise transfusions of blood given frequently and for a long time.

DR. E. GILLESPIE: The fact that lesions are found on the conjunctiva as well as in the mouth is an indication in favor of the diagnosis of pemphigus. Erythema multiforme may be confined to the mouth, but I have not seen lesions on the conjunctiva. The history of loss of weight also suggests pemphigus.

DR. H. T. PHILLIPS: I do not believe that this condition is pemphigus. It may be of toxic origin or it may be due to a fungus. Without lesions on the body or involvement of other mucous membranes, I do not see how a diagnosis of pemphigus can be verified.

DR. C. B. NORRIS: Taking into consideration the loss of weight and the absence of positive laboratory observations for Vincent's angina, it seemed to me that the diagnosis of pemphigus was apropos. The lesion about the umbilicus, while not a bleb, was not unlike cutaneous lesions that are seen in pemphigus. I should like to emphasize the giving of transfusions.

At this time I have a patient who has made no progress under treatment with massive doses of arsenic and tricophytin, as suggested by Sulzberger and Wise, but who has passed from a grave condition to an entire clearing up of all the blebs after three transfusions of blood, 500 cc. being given on each occasion.

Assuming that the case presented was one of erythema multiforme, I still believe that transfusions would be excellent for her.

DR. W. H. GUY: Dr. Guy said that he agreed with the diagnosis as presented. Dr. Jacob said that he had had a similar case in a minister. The lesions were limited to the nose and throat for one year, and then a single bullous lesion and Nikolsky's sign were found on the chest. The condition cleared up completely after six transfusions had been given. In the patient presented there were present circular erosions suggestive of a few preexisting lesions.

SCROFULODERMA. Presented by DR. FREDERICK AMSHEL.

E. S., a boy, aged 4, was seen for the first time on Sept. 13, 1932. An eruption had been present for more than a year. Anterior to each ear and over the zygoma there were two irregular, dime-sized, ulcerative lesions, the one on the right side being larger than that on the left. A sinus was present in each lesion. All forms of treatment had been applied to the lesions, without improvement. Two skin units of roentgen rays (unfiltered) was given, and in two weeks there was considerable improvement. Further roentgen therapy will be given later.

DISCUSSION

DR. W. H. GUY: Dr. Guy suggested that these lesions were sinuses which resulted from the incomplete closure of the branchial clefts. In support of this diagnosis was the fact that the father had the same type of lesion in front of the left ear. The treatment should be surgical.

DR. C. B. NORRIS: The suggestion by Dr. Guy that the trouble was caused by unclosed clefts (or possibly ductus endolymphaticus) is something that I had not thought of. The child is 4 years old, and this condition had been present for only one year. One would feel that preceding the ulceration evidence of cystic retention should have been noticed.

DR. F. AMSHEL: I did not think of Dr. Guy's diagnosis at the time of presentation. I cannot understand why these lesions should appear after the age of 3 years. Previous to the time the patient was seen by me, many remedies, such as caustics and curettage, had been tried. Ammoniated mercury was applied, with no results. Roentgen treatment improved the condition considerably. The patient was seen again in the clinic. The father stated that he had a foul-smelling discharge from the patulous opening in front of his left ear, and that his twin brother had a similar lesion anterior to the right ear. An opaque substance will be injected into the sinus, and a roentgenogram will be taken.

ACNE VULGARIS IN AN INFANT. Presented by DR. F. AMSHEL.

R. B., a boy, aged 7 months, presented many comedones on both cheeks and, to a lesser extent, on the forehead and chin. A few were also present in the ears. On the chin and, to lesser degree, on the cheeks were several papules and pustules. The mother stated that the eruption appeared when the patient was about 4 months of age, and that it had been present since that time.

DISCUSSION

DR. W. H. GUY: Dr. Guy said that he believed that the case was one of grouped comedones and not of acne.

DR. F. AMSHEL: When I first saw this patient I thought that the condition was a nevus, but the combination of comedones, papules and pustules situated only on the face suggested to me the diagnosis of acne vulgaris.

TERTIARY SYPHILIS (?). Presented by DRS. W. H. GUY and F. JACOB.

E. J., a colored girl, aged 15, presented a number of nodular, scaly lesions on both forearms and the backs of the hands, of one year's duration. These lesions began as small depigmented macules. Soon the centers became red and slightly scaly. This process continued until the lesions became lichenoid papules with depigmented areolae. Later lesions showed a heavy, adherent scale. A section taken for biopsy showed a granuloma which suggested syphilis, but was not characteristic. The Wassermann reaction was 2 plus. A mercury preparation given by mouth for two weeks caused definite improvement.

In favor of the diagnosis as presented were the nodular character of the lesions two weeks before presentation, the granulomatous character of the histologic picture, the response to therapy and the presence of a partially positive Wassermann reaction. The picture was unique if the history obtained was correct.

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Reporter*

Oct. 27, 1932

E. W. NETHERTON, M.D., *Presiding*

ESTHIOMÈNE (LYMPHOGRANULOMA INGUINALE). Presented by DR. H. F. DE WOLF.

M. D., a colored woman, aged 34, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, since 1924 had noted edema of the labia majora. For the past seven years she had had continuous dysuria. She was in Charity Hospital from Feb. 11, 1931, to March 8, 1931, for treatment. The following diagnoses were made: chronic hypertrophic vaginitis, with hypertrophy of the right labium majus and of the labia minora, and papilloma of the bladder, with acute hemorrhagic cystitis. The right labium majus was partially excised, and the labia minora seem to have been totally excised. Symptoms referable to the bladder had persisted and had become increasingly more severe. She had had some trouble in 1914 following the birth of her only child, but this seemed to clear up. There was no history of syphilis, and there were no miscarriages.

Examination gave essentially negative results, except in the genito-urinary system. The labia majora were edematous, and there was a linear scar extending the entire length of the right greater labium. The lesser labia were practically absent. Through the remnant of the right labium minus there was a small perforation. There was marked fibrosis of the clitoris. The urethra showed a definite stricture. Cystoscopic examination of the bladder showed a third degree cystitis. There was no evidence of old disease of the inguinal lymph nodes.

The Wassermann tests of the blood and spinal fluid gave negative results for syphilis. The urine showed the findings of severe cystitis. Frei tests were repeatedly positive. The phenolsulphonphthalein test was within normal range.

DISCUSSION

DR. H. F. DE WOLF: If this condition is given the name used in Europe, it must be understood to mean just the clinical picture in definite disease. For about seventy-five years this name has been used in Europe to describe ulcers of the vulva, with elephantiasis of the labia attributed to various conditions, one of them being tuberculosis. A few years ago it was discovered that many of these patients gave a positive reaction to the Frei test; so it must be that the virus which produces lymphogranuloma inguinale in the male is also responsible for this clinical disease in the female. I believe that there is very good evidence to support such a diagnosis in this patient. The Frei test has been definitely positive in several antigens.

DIFFUSE TYPE OF SARCOID OF BOECK AND PAPULONECROTIC TUBERCLE. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

Mrs. M. A. R., a white woman, aged 46, about two and one-half years ago noticed many button-sized lumps on the back of the hands and feet. She consulted a physician, who removed one of these tumors and sent it to Washington for examination. Following this, he gave her treatments with ultraviolet rays and later intravenous injections and treatments in the hip. She received the injections every day for a long period. Soon after they were started, an eruption began to appear; the skin became red and scaly. A blood test was made, but the results were not revealed to the patient. The injections were kept up until May, 1931, the cutaneous condition becoming progressively worse, and there is a history of extremely high fever during much of this time. In May, 1931, the treatments

were stopped; the patient immediately became better, and the fever was lower. The skin improved, and the patient gained 30 pounds (14 Kg.) in weight. The sores on the legs became worse, and in about January, 1932, she first noticed a rash on her face, which was symptomless but associated with high fever. The face became quite red and swollen. She had had three such attacks since January, 1932. A year previously an ulcer had developed on the conjunctiva of the left eye, which caused loss of sight in this eye.

There was a generalized eruption, with a diffuse, red, macular type of process. Over the face the process was a deep brownish red, with some induration of the tissue. Over the upper extremities, especially from the elbow down, the skin was very thin, hanging very much like a fine net. Over the hands and fingers there was a typical anetodermia, the blood vessels standing out clearly under the skin. There were certain punctate scars also over the upper limbs, and on the left arm there was a granulomatous mass about the size of a dime. The lower limbs showed a picture somewhat like that of the upper limbs, with numerous, sharply defined, punched-out ulcers, some of which were grouped below the knees; many grouped, pea-sized or slightly larger, sharply defined scars were distributed irregularly over the limbs. There was a certain amount of scaling which when the patient was first seen amounted to almost a dermatitis exfoliativa. The patient showed a corneal opacity of the left eye. She also had an ulcer of the bone of the septum of the nose, with ozena.

The Wassermann test of the blood was negative. Examination of the lungs and mucous membranes gave negative results. A biopsy specimen of the epidermis showed it to be thin, but slightly edematous. The stratum corium was somewhat thickened. The epidermis was flat. Throughout the corium could be seen young connective tissue infiltrated with cells, most of them of the mononuclear type. The vessels of the subcutis were thickened. There was evidence of caseous necrosis at one edge. There were numerous large giant cells of the Langhans type throughout the section.

DISCUSSION

Dr. John A. Gammel: I have never had an opportunity to see a diffuse type of sarcoid of Boeck. I think that the lesion and the multiple scars on the extremities resemble papulonecrotic tuberculids.

Dr. H. J. Parkhurst: I felt that there were many aspects of lupus erythematosus disseminatus in this case, especially as borne out by the lesions on the shins and by the eruption over the arms, where I found some follicular plugs. I have seen lupus erythematosus of this type associated with other tuberculids, which I think would fit in with a diagnosis of this case.

Dr. H. N. Cole: We have presented this patient with apologies. Thus far we have not been able to persuade her to go to the hospital for careful study. We even had difficulty in getting a small biopsy. The histologic appearance of this specimen as presented was that of a papulonecrotic tuberculid. I realize that the picture shown on the hands and forearms resembles somewhat acrodermatitis atrophicans, with the peculiar reddish appearance, the anetodermia and the atrophy. The patient shows, however, characteristic areas of papulonecrotic tuberculids on the lower limbs, from one of which a specimen for biopsy was taken. She also shows some deep ulcerations of the lower limbs, some of them with crusts, and over the face there is a rather diffuse, deep reddish-brown, somewhat indurated type of sarcoid. The face shows a certain amount of edema of the tissues, and the patient gives a history of having had several mild attacks of erysipelas over the face, with a final production of what I take to be an elephantiasis nostras. I appreciate the suggestion of Dr. Parkhurst that this might be a case of lupus erythematosus disseminatus. On the other hand, I have not seen a case of the disease lasting as long as this patient's has, nor showing a chronic deep ulceration such as this patient shows on the lower limbs. I think that the arms are an example of the end-results of a diffuse type of sarcoid of Boeck. The face shows

a typical sarcoid of Boeck, and the lesions on the lower extremities are an allied type of papulonecrotic tuberculid.

DR. H. G. MISKJIAN: What do you think is the relationship between the treatment she had and the eruption, high fever and other symptoms?

DR. H. N. COLE: I do not know what treatment she received, whether a gold compound or arsphenamine was given, but I do not think that treatment could explain the condition. When we first saw her she had exfoliative dermatitis as the result of treatment.

DR. M. J. GIBANS: I should like to question Dr. Cole regarding the etiology of the lesions on the legs?

DR. H. N. COLE: They are due to tuberculosis.

DR. R. E. BARNEY: Do you consider the lesions on the legs gummatous tuberculosis?

DR. H. N. COLE: Yes, I think some of the lesions look like a gummatous type of tuberculosis.

HEREDOSYPHILIS. Presented by DR. H. F. DE WOLF.

J. J., a girl infant, aged 3½ months, from the service of Dr. H. N. Cole and Dr. J. R. Driver, at Cleveland City Hospital, was born in Cleveland City Hospital on July 12, 1932, after a full term pregnancy. The mother was admitted to the dermatologic service on April 16, 1932, with active secondary syphilis. The infection evidently took place in January, 1932. The mother received 3.8 Gm. of arsphenamine and 0.15 Gm. of mercuric salicylate before delivery.

The Wassermann reaction with the cord blood was strongly positive. On July 30, 1932, the results of physical examination were essentially negative. A Wassermann test repeated on this date was strongly positive. Treatment with neoarsphenamine intramuscularly was started on Aug. 6, 1932. Three doses of this drug, each 0.02 Gm., were given up to Aug. 20, 1932, when the mother stopped bringing the infant for treatment. The infant was admitted to the pediatric service of the hospital on Oct. 22, 1932, because of a swollen abdomen and an eruption of five days' duration. She was transferred to the dermatologic service on Oct. 25, 1932.

Examination revealed palpable enlargement of the liver and spleen and a brownish, maculopapular eruption which was most evident on the extremities. The eruption was sparse over the face and body. The palms and soles showed only a few lesions.

The urine showed a trace of albumin and an occasional white blood cell. The white blood count at the time of admittance was 17,700. No serologic work has been done since July 30, 1932.

DISCUSSION

DR. SIDNEY LITTMAN: Congenital syphilis is always interesting, and in this connection I should like to mention two cases which I have seen recently. Children not only can be born with syphilis, but can contract it on passing through the birth canal. I saw a baby from 4 to 6 weeks old with a well developed primary lesion over the right eye. The mother had acute secondary syphilis. The child had probably acquired it during birth. I saw another baby, 6 weeks old, with a lesion over one zygoma. The lesion was hard and indurated, with no breaks in the continuity of the surface and no adenopathy. The diagnosis of a primary lesion did not occur to me at this particular time, but three or four weeks later a macular syphiloderm developed. The mother had palmar and plantar lesions, and the father was syphilitic. The obstetrician who delivered the baby said that at the time of delivery one of the blades of his forceps had slightly nicked the cheek. The lesion presumably healed, but a primary lesion later developed at this site. The mother apparently acquired syphilis late in pregnancy, and the child did not acquire it in utero, but contracted it at the time of birth.

DR. H. F. DE WOLF: I should like to speak about the distinction between heredosyphilis and congenital syphilis. Ordinarily, as I understand, congenital syphilis is acquired during birth, but in the case presented, I believe that the condition is true heredosyphilis, infection before birth, and therefore a disease inherited through the mother.

DARIER-ROUSSY SARCOID. Presented by DR. L. J. CARSON.

R. J. B., a white man, aged 26, six months before presentation, while folding his arms, felt nodules in the upper part of the right arm. These were not painful. Examination showed from six to eight subcutaneous nodules, varying in size from that of a match-head to that of a pea. The skin was slightly purplish over some of the lesions. The Wassermann test and the blood count gave negative results. The urine was normal. A section taken for biopsy was made up of miliary masses composed of epithelioid cells. These miliary masses were separated by narrow strands of lymphoid tissue. A pathologic diagnosis of tuberculosis of the skin was made.

DISCUSSION

DR. H. J. PARKHURST: I felt that the clinical features of this case were those of sarcoid.

DR. E. GILLESPIE: I believe that this patient would show improvement under roentgen treatment. I had one patient who showed considerable improvement after a second injection of gold and sodium thiosulphate, and was more than half improved after a few injections. I should suggest that such treatment be tried in this case.

DR. H. N. COLE: I did not see the section. Of course, much would depend on whether it showed the picture of tuberculosis or sarcoid. This condition could well be a tuberculosis of the hypodermia described by Wende.

DR. C. B. NORRIS: I remember showing a patient to Dr. La Rocco and Dr. Netherton, a man who had a lesion on the side of his face. A number of years ago, Dr. Wende had treated it with some escharotic agent. There was considerable scarring, and he had removed it. Six or seven months later I used gold and sodium thiosulphate without any beneficial effect, and I showed the patient to a physician who suggested that I use arsenic; I used this drug and since that time I have not given any other treatment. About a year ago I saw the man and treated him, and about six weeks ago the condition had entirely disappeared. Dr. Carson began treatment only six months ago; I wonder if he is patient enough.

DR. E. W. NETHERTON: I think I had the impression that the condition was clinically a sarcoid, which one occasionally sees on the arm.

DR. L. J. CARSON: I have seen many cases of Boeck's sarcoid, but very few of this type of sarcoid. Although I have used considerable roentgen therapy, both deep and superficial, and administered solution of potassium arsenite for three months, I do not see much improvement in the patient.

DISSEMINATED LUPUS VULGARIS. Presented by DR. E. W. NETHERTON.

A Negro, aged 23, first noticed an eruption nine months before this presentation. At the age of 17 he had acute arthritis. This was complicated with hydropericardium, for which he was operated on at Lakeside Hospital. At the age of 21, he contracted gonorrhea, which was not treated. He had been troubled with severe aches and stiffness in the lower part of the back, hips, knees and shoulders. There had been no objective symptoms. Roentgen examination showed a condensing osteitis of the lumbar spine, the wing of the sacrum and the adjacent portions of the iliac bones. The lower end of the right femur and the upper end of the tibia were also involved. No destruction or periostitis was noted. He had an aortic regurgitation and a chronic prostatitis. The Wassermann and Kahn

tests were negative on two occasions. He had a mild anemia and an increase in phosphatase in his blood. Chemical examination of the blood showed that it was normal. The patient refused to have a spinal puncture.

The eruption consisted of disseminated papules and plaques on the left elbow, nape of the neck, face, penis and scrotum. The papules varied in size from that of a large-headed pin to that of a match-head. The plaques were flat or linear, raised, smooth or nodular, slightly scaly and dull red, with some central depigmentation. All the lesions were infiltrated. On the elbow was one lesion with a verrucous surface, but no ulceration. The penis and scrotum were most involved. There was no abnormal enlargement of the superficial lymph nodes.

A specimen taken for biopsy from the left elbow showed some hyperkeratosis and some acanthosis. In the papillary layer and throughout the corium were well defined areas consisting of endothelioid cells, fibroblasts and small lymphocytes. The lymphocytes were more numerous around the periphery of these areas. In places there were well formed tubercles, with giant cells of Langerhan's type, but no areas of caseation. Sections stained for acid-fast bacilli were negative. Results of inoculation into guinea-pigs and cultures made from the tissue have not been reported.

Roentgenograms of the chest showed enlargement of the heart, particularly of the left ventricle (aortic regurgitation). Calcifications at the base of the right side were thought to be indicative of an old tuberculous process. Orthopedic diagnosis of "marble bones" or Albers-Schönberg disease was made. Biopsy section and roentgen plates were presented.

DISCUSSION

DR. R. E. BARNEY: My conception of lupus vulgaris is that it usually begins in the first decade and has a tendency to be localized to perhaps one area, progressing very slowly, with scarring. In this case, however, the dissemination more closely resembles sarcoid.

DR. H. N. COLE: I am very much interested in this case. As the man is colored, it is difficult to discern the color of the lesions. The histologic picture is that of foci of cellular infiltration and giant cells with connective tissue septums, and is suggestive of sarcoid. I should be inclined to agree with Dr. Barney that the lesions are a nodular type of sarcoid. I have seen only one case, in a colored woman. I should suggest that treatment with tuberculin in decreasing doses be tried; if the patient has anergy, it verifies the diagnosis of sarcoid. There might be allergy with lupus miliaris disseminatus.

DR. E. W. NETHERTON: The disease may be sarcoid of Boeck or a form of tuberculosis. The first factor noted by my associates and me was the general distribution of the lesions. We thought they were syphilitic, and I have been surprised that no one has thought of that today. We have also studied the section, and, as Dr. Cole says, there are one or two areas in it which we thought showed typical tuberculids. We used some tissue for inoculation of a guinea-pig, with a result thus far negative. As far as lupus vulgaris is concerned, I am under the impression that disseminating lupus vulgaris can occur in adults. In one patient whom I saw, a man who was shot in the chest during the World War, what I thought was lupus vulgaris developed, involving the face and neck; there were several lesions over the body. This condition had started shortly after the war.

DR. H. N. COLE: This patient also shows changes in the bone. Would there be such changes as he shows with lupus miliaris?

A CASE FOR DIAGNOSIS. Presented by DR. E. W. NETHERTON.

A priest, aged 56, whose past history was unimportant except for a thyroidectomy for an adenomatous goiter in February, 1929, had an eruption on the anterior surface of the legs about nine months before this presentation. The condition

appeared as a brownish-red discoloration on the left shin. There have never been any subjective symptoms. This discoloration gradually increased, and the skin became thickened. The right leg became involved several months later than the left.

On the anterior surface of the lower third of each leg there was a chronic, thickened, nodular plaque of a solid, edematous condition. The surfaces of the lesions were glossy and brownish red. Some retraction of the surface of the skin at the follicles gave a pigskin appearance. In some areas of these plaques there were small, round, whitish papules which looked like vesicles, but were found to be solid when incised. The face was ruddy, suggesting polycythemia.

Blood counts showed 5,500,000 red cells, 5,200 white cells and 97 per cent hemoglobin. The Wassermann and Kahn tests were negative. The basal metabolic rate was — 12 per cent. A biopsy specimen taken from the left leg in June, 1932, showed the following changes: There was no noteworthy change in the epidermis. There was a mild, inflammatory reaction in the papillary layer of the corium. The collagenous fibers in the corium were edematous; they were widely separated, with nuclei sparsely separated. In the subcutaneous tissue there was considerable, rather homogeneous, pale-staining material, probably of a mucinous nature.

DISCUSSION

DR. R. E. BARNEY: I have only two suggestions to offer: that the condition is either the edematous stage of scleroderma or a possible colloid degeneration of the skin.

DR. H. J. PARKHURST: On palpation the nodules were quite firm. There was no tenderness or erythema, and the nodules were symmetrical. I believe that both points indicate an early case of erythema induratum.

DR. H. N. COLE: I have been watching for one of these cases ever since O'Leary's article was published (ARCH. DERMAT. & SYPH. **21**:57 [Jan.] 1930). He has written mostly in regard to the myxedema occurring on the shins after thyroidectomy. It is a rare and interesting condition, and I appreciate the opportunity of seeing this patient.

DR. E. GILLESPIE: Is this case similar to that shown at Philadelphia and reported by Pillsbury and Stokes (ARCH. DERMAT. & SYPH. **24**:255 [Aug.] 1931)?

DR. H. N. COLE: Yes.

DR. SIDNEY LITTMAN: I saw a patient with a condition similar to this, with acute involvement. Dr. Crile had operated on him and made this diagnosis.

DR. J. EDGAR FISHER: Why is this condition so rare if it is seen after thyroidectomy?

DR. E. W. NETHERTON: I do not know. This is the second case that we have seen in many thyroidectomies; at least it is only the second one that has been called to my attention. There may have been more. As Dr. Cole says, O'Leary was the first to describe the condition following thyroidectomy, but one or two cases were seen in patients with hyperthyroidism. They do not respond to any therapy, internally or locally.

DR. C. J. SHEPARD: Will the lesions remain localized?

DR. E. W. NETHERTON: As I remember, they remain localized and on the lower extremities.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

D. H., a colored man, aged 21, was admitted to the Cleveland City Hospital, to the service of Dr. H. N. Cole and Dr. J. R. Driver, on Sept. 28, 1932, complaining of marked swelling of the inguinal lymph glands which had developed following a urethral discharge of six weeks' duration.

On admission to the hospital, the penis was edematous and, at the prepuce, markedly phimotic. There was a shallow ulcer about 8 mm. in diameter on the edge of the prepuce. There was considerable purulent discharge from the preputial sac. There was a hard, indurated mass of glands in each groin measuring approximately 6 by 12 cm. On the summit of each mass there was a broken-down ulcer about 2 cm. in diameter. These enlarged masses were not tender to palpation. The Frei test was positive. The Wassermann test was slightly positive (1 plus).

The patient had received a total of 63 cc. of a 1 per cent solution of antimony and potassium tartrate since Oct. 4, 1932, and considerable improvement had resulted.

PERIANAL GRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

J. B., a white man, aged 30, was admitted to Cleveland City Hospital, to the service of Dr. H. N. Cole and Dr. J. R. Driver, on Oct. 4, 1932, complaining of a perianal growth which had started about twelve years previously. He had practiced sodomy and other forms of sexual perversion for many years. A diagnosis of syphilis had been made several years previously, but antisyphilitic treatment did not prevent further extensive development of the lesion. In 1929 the lesion was diagnosed as condyloma acuminatum and was removed surgically in another hospital. The patient had had a chancre in 1919 and gonorrhea in 1920.

Examination revealed a large granulomatous lesion about 9 cm. in length by 5 cm. in width, involving the perineal, perianal and intergluteal region. The edges were raised, indurated and had a rolled-over character, while in the midline there was ulceration, with a beefy red base. General physical examination otherwise gave negative results.

A Wassermann test of the blood was negative. The result of a precipitation test for syphilis (Kline) was four plus. The spinal fluid was normal. Tissue smears were positive for Leishman-Donovan bodies. The formaldehyde-gel test was strongly positive in five hours. The Frei test was negative. The patient was under treatment with intravenous injections of a 1 per cent solution of antimony and potassium tartrate, and to date had received a total of 38 cc. Definite improvement was reported.

DISCUSSION

DR. J. E. RAUSCHKOLB: I believe this is the first case of granuloma inguinale I have seen in a white person. All the cases I have seen have been in colored people. There is no inguinal adenopathy to assist in a diagnosis of granuloma inguinale, because granuloma inguinale is a disease of the skin, as compared with lymphogranuloma inguinale described by De Wolf and Van Cleve in a recent issue of *The Journal of the American Medical Association* (**99**:1065 [Sept. 24] 1932). When this man was first seen, we thought of the possibility of a gumma. The Frei test was negative, ruling out lymphogranuloma inguinale. The finding of Donovan's bodies in the smears makes a diagnosis of granuloma inguinale positive. I believe that with the therapy instituted, antimony and potassium tartrate, the patient has shown considerable improvement since he was first seen.

DR. H. N. COLE: This is the second white person we have had in the clinic with granuloma inguinale. Right after the World War we saw our first case in a white woman with a possible strain of colored blood, of which, however, there was no evidence. The picture this man presents is quite different from that of condyloma acuminatum around the anus. The fact that the lesion, instead of being wartlike, was hard, quite indurated, pearly and rolled-over made me suspicious of granuloma inguinale. The examination for Donovan's bodies gave positive results, confirming the clinical diagnosis.

ATLANTIC DERMATOLOGICAL CONFERENCE

R. L. GILMAN, M.D., *Secretary*

Philadelphia, Nov. 11, 1932

F. D. WEIDMAN, M.D., *Presiding*

POIKILODERMA VASCULARE ATROPHICANS. Presented by DR. S. S. GREENBAUM.

M. S., a white man, aged 58, was admitted to the Mount Sinai Hospital on Oct. 12, 1932, with a chief complaint of redness and slight itching of the skin. The condition had existed intermittently for twenty-five years, starting on the chest as a macular lesion, 6 cm. in diameter, containing red spots and whitish areas. This lesion disappeared and recurred several times, and then similar areas appeared in other parts of the body, avoiding the face, forearms, buttocks and perineum. There were no mucosal lesions. These lesions remained quite constant, occasionally showing an inflammatory areola. The history was otherwise negative except for hay fever in 1912 and a "nervous breakdown" in 1923.

The patient had a blood pressure of 180 systolic and 110 diastolic, diseased teeth, apical fibrosis, enlargement of the heart to the left, with a systolic apical murmur and an accentuated aortic second sound, and peripheral sclerosis. The skin showed numerous pink scaly lesions on the trunk and lower extremities. Some of these pink lesions had white, lentil-sized atrophic areas intermingled with numerous, red telangiectases, the size of a pinhead. In some of the clearly defined lesions there was a raised border, giving the central area a depressed appearance.

The results of a blood count and urinalysis and chemical analysis of the blood were normal. The Wassermann reaction was negative. The blood phosphorus on two occasions was low (1.9 and 2.0 mg.), but a third reading was normal (3.1 mg.). The sedimentation rate was normal. A liver function test (bromsulphalein) gave a normal result. A phenolsulphonphthalein test showed excretion of 48 per cent of dye somewhat diminished. A sugar tolerance test revealed a diabetic tendency. A roentgenogram of the skull showed a normal-sized pituitary fossa and decalcification in the left parietal region with prominent striae.

POIKILODERMA VASCULARE ATROPHICANS. Presented by DR. S. S. GREENBAUM.

N. P., a white man, aged 42, presented an erythematosquamous eruption, not itchy, limited largely to the upper and lower extremities, ears and eyebrows. On the lower extremities it was mottled pink, with moderate scaling of lamellar type. Red lesions, the size of a pinhead or slightly larger, appeared on the thighs and legs. On the arms there were numerous red puncta in addition. Similar palm-sized patches occurred on the chest. Both extremities, upper and lower, showed acrocyanosis. There was a small scar on the corona glandis, the result of a lesion that had appeared four weeks previously. This lesion gradually healed spontaneously. There were scattered telangiectases on the eyelids, lip, palate, foreskin, etc.

There was a history of a four plus Wassermann reaction obtained elsewhere, unconfirmed at the Mount Sinai Hospital. A biopsy by Dr. Weidman was reported as follows: "Histologically the sections were not distinctive. They showed what appeared to be a thinning of some of the prickle cells at certain points, which was the only thing that could be translated into an atrophy. The horny layer was in perfect shape." Clotting time was five minutes; bleeding time, one-half minute. On Jan. 11, 1932, a biopsy was reported as showing "a small amount of perivascular mononuclear infiltration with scattered cells in the papillary portion of the corium and adjacent corium tissue." On January 29 the blood cholesterol was 192 mg.; on April 1, 224 mg.; on October 7, 240 mg., and on October 14, 250 mg.

The patient had been well until seven years previously, when small lesions appeared on the face, arms and thighs. The rash healed while the patient was taking light therapy, but recurred after treatment was discontinued. No treatment

had been given for the past six years. On exertion or exposure to the sun he perspired freely, but almost entirely on the head. Longer exposures to the sun produced exhaustion from heat, whereas previous to the development of the rash he was never so affected. In July, 1932, the eruption markedly improved on the part of the body well tanned by the sun. In October there was marked improvement, particularly over the semiburnt areas above the waist. Many of the telangiectatic areas disappeared. Inflammatory papules the size of a pinhead were still present here and there on the trunk. There was no pruritus.

DISCUSSION

DR. G. M. MACKEE: These cases are the best examples of poikiloderma vasculare atrophicans that I have yet seen. As John Lane has so often remarked, the typical eruption of this disease resembles the lesions of so-called "x-ray skin"—atrophy, telangiectasis and pigmentation, all of which were seen in large areas, particularly in one of the patients. There is some clinical evidence to support the contention that poikiloderma is a prefungoid stage of mycosis fungoides in spite of the fact that the pathologic histology of poikiloderma does not suggest any form of lymphoblastoma. However, the same is true of other types of prefungoid mycosis fungoides, as for instance when the prefungoid stage cannot be differentiated, clinically or histologically, from eczema or psoriasis.

ECZEMATOID PARAKERATOSIS OF HERXHEIMER; LEVURID OF RAVAUT. Presented by DR. J. H. STOKES.

E. B., a white woman, aged 46, presented a chronic intertriginous dermatitis limited to the toes, groins, left popliteal space, inframammary regions, flexures of the elbows, ears and lid margins. The lesions in the groins exhibited vegetations, almost condylomatous in type, with narrow keloidal scars extending from 3 to 4 inches (7.6 to 10.1 cm.) along the inguinal furrow. Superficial ulceration was noticed at times, with bright red granulation tissue evident at the points of contact of the scars and skin. The external genitalia were swollen, with an indurated, glistening white skin extending posteriorly along the anus and up the intergluteal cleft.

A biopsy showed moderate epithelial hyperplasia with granulation tissue and some polymorphonuclear infiltration. There was no histologic evidence of tuberculosis or syphilitic granulomas. Smears were negative for Donovan bodies and tubercle bacilli. The Wassermann reaction of the blood was negative. A smear from the bend of the elbow showed some small ovoid forms compatible with Pityrosporum ovale; otherwise no fungus was grown from the various areas of involvement. Animal inoculation gave negative results for tuberculosis. Two blood cultures were sterile, but on the third attempt a short-chain streptococcus was found. Culture from blister fluid also showed a short-chain streptococcus. From the intertriginous areas the following organisms were cultured: hemolytic Staphylococcus aureus, hemolytic Streptococcus anginosus, hemolytic Streptococcus equi, and a nonhemolytic Streptococcus ignavus.

The patient was first seen in May, 1931, at which time a history was obtained of a dermatophytosis of the toes of five years' duration. Involvement of the groin occurred three years later, and subsequently the other sites of distribution became affected. The patient progressively lost weight and showed other evidences of a marked constitutional reaction in the form of malaise, weakness and general increasing debility.

From the standpoint of treatment the entire gamut has been run: intravenous injections of sodium thiosulphate, the local use of gentian violet, Castellani paint, potassium permanganate douches, roentgen and general light therapy, sodium eosinate, antimony and potassium tartrate, theelin and the intracutaneous injection of an autogenous streptococcus vaccine. The last-mentioned form of treatment produced a striking temporary improvement. The test injection produced a marked local and general allergic reaction, as in Ravaut's cases. After the patient had

obtained a three-fourths involution of the process, a standstill developed; this was followed by the use of schizosaccharomycin (Benedek), which caused a local as well as a general reaction, but did not produce a focal flare-up immediately following the first few injections. A new streptococcus vaccine resulted in a focal flare-up with slight clinical improvement. Bacteriophage has been considered, but up to the present has never been used. Recently in an attempt to increase the patient's weight by a more liberal carbohydrate diet, insulin has been added to the aforementioned methods of therapy.

DISCUSSION

DR. J. H. STOKES: This case is the worst, or the best and most extreme, example of this condition that I have seen, and is in certain respects unique. The vegetations in the groin I have never seen before in a picture of this kind in a group of cases that I have been collecting in my practice for several years. When I was abroad, two years ago, I was in such a state of perplexity that I talked about the Continental conceptions of this picture with Pautrier and Bloch, and I found that it was by no means a novelty to them; from as accurate a description of the condition as I could give at the time, I found that it was apparently identical with the eczematoid parakeratosis of Herxheimer. That is simply a name, of course, applied to this intertriginous process which Ravaut has gone into more deeply of late; according to his conceptions, it consists of streptococcal allergic secondary lesions superimposed on an underlying mycotic process. This patient furnished us with the first analysis of this conception with which I am familiar in this country. The patient has had the condition for a number of years. Dr. Weidman was unable to isolate a fungus, although we hoped that we would find one to complete the Ravaut picture. Our bacteriologist at the University Hospital, Dr. Lynch, succeeded in collecting three types of streptococci and one staphylococcus. This patient showed a striking allergic intracutaneous reaction and systemic reaction to the injection of this mixed group of organisms, but particularly to Streptococcus equinus. The condition conforms to the Ravaut picture to the extent that the patient has a mycotic-looking eruption with a typical pyogenic streptococcic infection superimposed thereon, to which she reacts allergically. This is the possible explanation of the persistence and the practical failure of this condition to respond to treatment. About eight months ago the autogenous streptococcal vaccine almost cleared up the condition. Then the patient began to react to the vaccine. It was impossible to get the dosage above a certain point. Retreat and starting over did not have any effect. The patient then was treated with a schizosaccharomycin which Dr. Weidman obtained through Benedek, and with the initiation of that treatment the condition retrogressed even more strikingly, returning to the present stage. An injection of the schizosaccharomycin resulted in nodule formation at the site of each injection, the nodules persisting for weeks. I think that the condition might have gone backward irrespective of the schizosaccharomycin. I should be glad to have therapeutic suggestions.

DR. G. M. MACKEE: The case seems to be unique in one aspect, namely, the ulcerative lesions in the crural region. Otherwise I have seen many cases that would fall into this category. It is often necessary to exclude psoriasis and seborrheic dermatitis, which has been done in this case. I agree with Dr. Stokes that the eruption is probably caused by fungi or pyogenic bacteria, or both. It is difficult to add anything to the therapy which has been so thoroughly and comprehensively tried in this case. My best results have been obtained with continuous wet dressings of very weak silver nitrate solution, 0.25 per cent. They must be continuous for two or three weeks, and the wet gauze must come in contact with every millimeter of the skin. Later, chrysarobin ointment may be tried, beginning with one-half grain (0.03 Gm.) to the ounce (28.35 Gm.) and increasing the strength according to toleration.

DR. PHILIP BURNETT: In a case that we had a number of months ago, the condition started in the groin, and the ulceration had extended onto the vulva when we saw it. We tried many methods of treatment including bacteriophage,

without result. On the suggestion of a colleague we commenced the use of insulin compresses (single strength unit, pure), and in two or three weeks the process had cleared up entirely. There has been no tendency to recurrence up to the present time.

Dr. L. W. Ketron: I feel that one should be cautious in drawing conclusions concerning the etiologic significance of an organism obtained from a cutaneous lesion because the patient shows a marked local or general allergic reaction to a vaccine made from this organism. Several years ago I made many tests in cases of acne with both a vaccine and a filtrate from the acne bacillus. There was no regularity whatever in the size of the local reactions in patients with acne, and in general they reacted to no greater degree than the same number of controls. I have seen a local reddened area varying from 1 cm. to the size of a hand and involving most of the flexor surface of the forearm. Lately I have been testing patients with various cutaneous eruptions with a staphylococcic filtrate which Dr. Burky in the Wilmer Institute has been using. Here also one sees a marked variation in the amount of local reaction which does not seem to depend on whether or not the patient has a staphylococcic infection of the skin. The most marked reaction that I have seen was in a patient who had no evidence of any cutaneous infection whatever. The entire arm became swollen, with a reddening over most of the flexor surface and a moderate lymphangitis.

Granuloma Annulare. Presented by Dr. Abram Strauss.

R. M., a white woman, aged 39, presented annular lesions on the anterior surface of both forearms, of two years' duration. The right forearm showed a circular lesion, about 15 cm. in diameter, with an elevated incomplete margin and a slightly scaly surface. There was no history of tuberculosis or of any previous acute illness except an ectopic pregnancy. Physical examination yielded essentially negative results. Roentgen therapy has markedly improved the appearance of the lesions. The Wassermann and other tests of the blood gave negative results.

DISCUSSION

Dr. Frederick Summerill: Clinically and pathologically this case appears atypical of granuloma annulare in that there is a greater amount of inflammation limited to the surface stratified epithelium than in typical cases. The lesions on the right arm are more comparable, and biopsy might show deeper extension of a chronic inflammation and fibrosis. Could not mycotic infection be considered to present this atypical picture?

Dr. L. W. Ketron: The most striking thing about granuloma annulare is the typical necrosis which may be found in most of the histologic preparations. In the patient under discussion, however, the section showed a cellular infiltration which had invaded and replaced to a great extent the rete pegs, leaving, however, their normal outline. This part of the picture resembled very much the changes in the sections from a patient whom I presented at the meeting of the American Dermatological Association in Montreal as "multiple lesions of the skin apparently of epithelial origin resembling clinically mycosis fungoides." Those who discussed this case felt that it showed mycosis fungoides and not an epithelial tumor. If these impressions are correct, I believe it quite likely that the case under discussion is also one of mycosis fungoides.

Dr. G. M. MacKee: We must take into consideration that the patient received roentgen therapy, which may have modified the picture considerably. It is not certain in what stage of evolution the biopsy was taken. This also should receive consideration.

Dr. F. D. Weidman: I felt that there were not sufficiently definite granulomatous changes in the corium to be compatible with the accepted histologic picture of granuloma annulare. At present the changes are more those seen in Bowen's

disease or in Paget's disease, but these diseases must be ruled out in view of the clinical features. Now that Dr. Ketron has reminded us of his case it appears to me that the most likely diagnosis is that of granuloma fungoides, particularly since, as Dr. MacKee stated, roentgen therapy may have modified the picture.

LUPUS ERYTHEMATOSUS AND GRANULOMA ANNULARE. Presented by DR. S. S. GREENBAUM.

R. R., a white girl, aged 4 years, was first seen on June 24, 1932, when examination revealed erythematous, slightly scaly patches over both cheeks, extending over the bridge of the nose, and infiltrated, annular, elevated, coin-sized plaques on the hands and arms resembling closely the lesions of granuloma annulare.

At the age of 15 months a reddish area appeared on the bridge of the nose, and the mother applied alcohol without any result. The child was taken to the shore later, and the following day it was observed that the redness had spread to the entire nose. During the following week it spread to the forehead, cheeks and lips. A doctor was consulted, who treated the condition as eczema for the entire summer. There was some improvement when winter came, and the lesions almost entirely disappeared. The following year the eruption on the face returned as soon as warm weather set in. Ultraviolet rays were applied for six months and the eruption then began to spread to the backs of the hands. During the summer of 1932 the eruption appeared on the forehead.

On June 24, 1932, weekly injections of gold and sodium thiosulphate were instituted. By October 19, 1932, fully 90 per cent of the facial rash had disappeared. Up to this time the patient had had seventeen injections of gold sodium thiosulphate in 25 mg. doses.

At the time of presentation the child was also under treatment for infantilism in the pediatric clinic, where she received thyroid extract and syrup of ferrous iodide.

DISCUSSION

DR. H. H. HAZEN: One of the cases today, that of granuloma annulare, was associated with a lupus erythematosus. I have seen two cases recently in which a granuloma annulare was associated with typical papulonecrotic tuberculids, and I am wondering if we cannot add granuloma annulare to the general group of so-called papulonecrotic tuberculids. Clinically it looks as though it might belong to that group.

DR. P. E. BECHET: I am treating at present a young woman of 23 with an extensive lupus erythematosus of exactly the same degree as that in Dr. Greenbaum's patient; it began after a severe sunburn. The child presented has the same history. I have not infrequently observed lupus erythematosus after prolonged ultraviolet irradiation. I believe that the incidence of lupus erythematosus following exposure to sunlight is not uncommon, and has not been sufficiently stressed. It is one of the real dangers of the popular sunbath of today.

CUTANEOUS NEUROMA. Presented by DR. J. B. LUDY.

M. J., a Negro, aged 37, presented on each arm and leg from fifteen to twenty deeply pigmented, discrete, firm, flattened tubercles varying in size from that of a split pea to that of a hazelnut. Several showed umbilication; they were firmly incorporated in the skin and diffusely distributed, and they did not follow any nerve trunk.

The lesions first appeared six years before, new ones gradually appearing. Except for occasional periods of mild itching they were symptomless until three years before presentation, when the patient came under observation. He then had severe spells of itching, knifelike pain and tenderness, whereas at other times the lesions were neither tender nor painful.

DISCUSSION

DR. H. H. HAZEN: I have heard a number of alternate diagnoses suggested, including that of prurigo nodularis by Dr. Mook. In cases of cutaneous neuroma and prurigo nodularis that I have seen the appearance is practically identical, with one exception, which is that cases of prurigo nodularis show many more scratch marks. I did not have a chance to study the section carefully, but I am wondering if the lesions could not be a pure fibroma. My impression is that the neuroma invariably causes more tenderness than pressure on these growths elicited.

ACANTHOSIS NIGRICANS. Presented by DR. J. B. LUDY.

V. C., a white girl, aged 16, presented dark skin of the face which shaded into darker, thickened area over the chin and lower lip. The circumoral skin was thickened, furrowed, and finely segmented. The antecubital regions were more affected than any others on the arms. The skin of the abdomen showed more involvement than the other portions of the torso. The groins, perianal and perivulvar regions were deeply pigmented and the skin thickened, as were the popliteal spaces.

One sister had pulmonary tuberculosis. This patient had an appendectomy in 1927. The skin disorder began ten years before presentation, as a black discoloration in the region of the forehead, around the mouth and over the back of the neck. The parents attributed it to an accidental application of oil and gasoline to the face and neck followed by sunburn. Since then the pigmentation has spread over the body.

ACANTHOSIS NIGRICANS. Presented by DR. J. M. SCHILDKRAUT.

N. A., a white woman, aged 41, presented a mottled pigmentation of the neck, axillae, groins, region under the breasts, wrists and backs of the hands. The pigmentation was grayish brown on the neck, and grayish black on the backs of the hands; at the latter site there were a few small surface nodules. The pigmentation under the breasts and in the groins was distinctly black. The skin was warty but soft to the touch.

The Wassermann reaction of the blood was negative. Some time before presentation, arsenic was found in the urine, but there was no definite history of arsenic intake, and the percentage was not computed. A biopsy on tissue from under the left breast showed hyperkeratosis, acanthosis and proliferation of the papillae, with hyperpigmentation in the deep layers of the epidermis. Some pigmentation was present in the corium just underlying the epidermis.

The condition started ten years before, on the neck; two years later it appeared under the breasts, and gradually developed on the other involved areas. The previous medical history was not significant, except for an appendectomy four years before. About nine months before presentation, the gallbladder was drained.

ACANTHOSIS NIGRICANS. Presented by DR. H. U. NORTH.

J. C., a white woman, aged 23, presented an eruption of the axillae and chest. In the axillae the lesions were soft verrucae, closely grouped. The eruption on the chest was a brownish macular condition with fine furfuraceous scaling. The patient sweated a great deal in these regions. The eruption had been present in the axillae for twelve years and on the chest for two months.

DISCUSSION

DR. G. M. MACKEE: There is no question about the diagnosis of acanthosis nigricans in these cases. One patient had a very mild eruption limited largely to several flexures. In this case, before accepting the diagnosis as unequivocal, it will be well to rule out fungi as the cause. We recently had a patient at the New York Postgraduate Skin Clinic who had an eruption very similar to this one, and in the same areas. We thought of a beginning acanthosis nigricans, but

we isolated a fungus, a monilia, I think, and while we have not determined the condition definitely, we think that it is a moniliasis that resembles acanthosis nigricans.

DR. J. M. SCHILDKRAUT: Probably owing to the lack of sufficient privacy the eruption was not seen in its entirety. From the character of the eruption in the groins and under the breasts I think that it is typical. It is definitely black, verrucous and soft. The microscopic section also indicates acanthosis nigricans.

SCLERODERMA CIRCUMSCRIPTA (?). Presented by DR. C. S. WRIGHT.

W. E., a white man, aged 21, presented the typical hidebound appearance and physical characteristics of scleroderma. The areas were sharply circumscribed and slightly erythematous. The lesion on the right leg measured 20 by 10 cm.; that on the left leg, 7 by 10 cm. The patient first noticed a hard, reddish spot, 1 cm. in diameter, on the anterior aspect of the lower third of each leg in June, 1932. About a month later another similar spot developed on the inner aspect of the lower third of the right leg. The first two lesions spread rapidly.

He had a subtotal thyroidectomy on Sept. 29, 1931. The pathologic findings at the time of operation were: "Gland enlarged and seat of adenoma about the size of a walnut; fatal adenoma of thyroid, showing marked epithelial hyperplasia." The Wassermann reaction of the blood was negative.

The report on a biopsy read: "The epidermis is thin; the papillae well formed; cells of stratum germinativum are vacuolated. The corium immediately below the epiderm consists of closely packed fine fibers lying between coarse wavy hyaline fibers of collagen. In the deepest portion of the section are closely packed, coarse, wavy hyaline fibers only."

DISCUSSION

DR. D. M. PILLSBURY: It seems to me that the characteristics of this case, namely, a doughy, raised infiltration, sharply limited to the pretibial areas, and its pigskin-like appearance, coupled with the association with thyrotoxicosis make a diagnosis of circumscribed myxedema almost inescapable.

DR. F. D. WEIDMAN: I thought the same thing when I first saw the patient, and I think that the sections confirm it. The tissue is reticulated and the granules in the meshes take a very definite deep blue color which is quite compatible with the reaction which subcutaneous mucin gives.

ZOSTERIFORM SCLERODERMA. Presented by DR. F. D. WEIDMAN.

This case was reported in the ARCHIVES for the March, 1932, issue, p. 560.

DISCUSSION

DR. F. D. WEIDMAN: This patient showed marked improvement under atropine therapy, which was prompted by the obvious nervous character of the disease, with its zosteriform distribution. Ramisection was considered for a while as a possibility, but it was thought advisable to try other methods first, and it appears that improvement has taken place so rapidly that it will not be necessary to resort to surgical procedures.

ALOPECIA TOTALIS. Presented by DR. J. V. KLAUDER.

E. M., a white boy, aged 12 years, was first seen in April, 1932, presenting alopecia totalis. He was given hydrolized wool by mouth, 2 teaspoonfuls three times daily. About two weeks later, fine hairs appeared on the scalp, and the growth of hair continued. At the time of presentation the patient showed obvious regrowth of hair over the entire scalp, eyebrows and face. The administration of hydrolized wool had been continued since April. The only other treatment was the application of ultraviolet rays to the scalp every three or four weeks.

TWO CASES OF ERYSIPELOID. Presented by DR. J. V. KLAUDER.

F. M., a white man, aged 22, presented erysipeloid two days after scratching the third finger of the right hand on a hog bone. Treatment consisted of ichthyol, 12 per cent in alcohol, and intensive applications of ultraviolet rays. This treatment was ineffective, and the infection gradually spread. After an injection of 8 cc. of swine erysipelas serum the infection improved considerably.

J. P., a white man, aged 48, scratched the right side of his hand Nov. 7, 1932, while handling hogs. A well pronounced erysipeloid appeared at this site two days later, involving the entire right side of the hand and extending onto the dorsum of the hand and the distal parts of the fourth and fifth fingers. Ten cubic centimeters of the bacillus of swine erysipelas serum was injected in and around the lesion on November 10. By November 11 the infection was 50 per cent improved, and showed the usual swelling in the region of the infection following an injection of serum.

SIX CASES OF MULTIPLE EPITHELIOMAS AND TWO CASES OF KAPOSI'S SARCOMA. Presented by DR. G. E. PFAHLER.

To conserve space, these six cases were not abstracted.

DISCUSSION

DR. G. E. PFAHLER: The cases were presented to show the likenesses and differences in the condition of the skin. One patient had an extensive group of lesions which had been growing for about forty years, ranging from precancerous lesions to basal cell or squamous cell carcinoma, and varying in size from that of a pinpoint to that of a fist. Another patient who was shown had extensive pigmentation together with keratoses, basal cell carcinoma, squamous cell carcinoma and a group of metastatic lymph nodes, some of which had been removed. Is there anything that would tend to modify the underlying soil in the tissue and prevent these lesions from developing or recurring? In four of these patients, to whom cod liver oil and calcium gluconate were given the skin has changed from a dry, scaly type which had been present for many years (one man said all his life) to one of smooth, soft texture. If one can change the texture of the skin in such a manner that the lesions will not develop in the future, something very definite will have been accomplished.

In two or three of these cases an effort was made to modify the soil by the injection of solutions of hydrochloric acid, beginning with 1:1,500, then 1:1,000 and increasing concentrations to 1:200. In one of the cases local injections into the skin were given; in the others intravenous injections. No change could be observed in the skin.

The cases of hemorrhagic sarcoma (Kaposi's disease) were shown because all the lesions that were treated were eliminated. Most of these lesions were removed by electrothermic desiccation; some by dissection, so as to get biopsy material. A group developed that was too large to be removed by that means; these were treated with roentgen rays, and this treatment has been continued.

Dr. Case showed the microscopic specimens from these cases, and from a case of hemorrhagic sarcoma that developed eight years after the removal of the patient's breast and six years after she had been treated successfully for recurrent carcinoma. During the past year extensive edema of the arm developed, and on this edematous arm numerous blebs or lesions appeared which, when studied by Dr. Case, were pronounced hemorrhagic sarcoma.

DR. E. A. CASE (by invitation): The etiology of these cases of multiple epithelioma is obscure. There is some tendency which predisposes to the development of these tumors, and interestingly enough, many of them last for years. Another interesting feature is that in these cases, while one finds various types of carcinoma, the vast majority of them are of the basal cell type (67 per cent), only 10 per cent being of the squamous cell type. In two cases of this series there were both types of carcinoma. In the case of the woman with sarcoma who

had had cancer of the breast, we did not think that the condition was Kaposi's disease, but believed it to be a hemorrhagic sarcoma. Perhaps that is a poor name to give it.

DR. J. J. ELLER: The report that the ingestion of cod liver oil will improve the texture of the skin is interesting. Biochemists explain that the texture and health of the skin are maintained by cholesterol and glucothione, the latter being active in aiding the metabolism of skin cells. The cholesterol which is found in sebum counteracts dryness and detoxicates. Glucothione is found in yeast, eggs and milk. I believe that a better way of improving the skin texture and skin metabolism would be to apply some preparation containing the cholesterol, such as hydrous wool fat, and also perhaps by increasing the ingestion of foods containing large quantities of glucothione.

DR. FRED WISE: We treated most patients with Kaposi's sarcoma by means of unfiltered roentgen rays. At the suggestion of Dr. John Remer we experimented with filtered roentgen rays, and in several obstinate cases procured good results. Most of the results, however, were temporary. I can recollect only one patient who was really cured after a number of years.

DR. F. J. EICHENLAUB: Until more is known about the etiology of new growths, I think the assumption that changing the texture of the skin, even if we succeed in doing it, is going to make a difference in the development of epitheliomas is not likely to prove of value.

DR. G. M. MACKEE: Assuming that Dr. Pfahler is correct in ascribing the improvement to the ingestion of cod liver oil, this effect may be due to the correction of a vitamin deficiency rather than faulty cholesterol metabolism. It might be a good plan for more dermatologists to try the same method over a period of years and see if this treatment will modify a presenile skin or a sailor's skin. His collection of cases is interesting also from the standpoint of multiformity of lesions. Some pathologists aver that there never is a carcinoma without an antecedent lesion of some kind. At the other extreme we have pathologists who think that carcinomas are never preceded by antecedent lesions. These cases indicate that many carcinomas of the skin are preceded by such lesions. Such able dermatologists as Jadassohn and Bloch, for instance, think that most carcinomas of the skin are preceded by precancerous conditions, and that these precancerous conditions do not always lead to the same type of carcinoma. For example, a seborrheic keratosis or a senile keratosis may produce any one of the three recognized types of cutaneous carcinoma, or may lead to Bowen's disease, and again Bowen's disease may remain as such or may change to basal or squamous cell carcinoma. I do not suppose that one should discuss a discussion, but there is no mystery about the greater efficacy of filtered radiation as compared with unfiltered radiation. With filtered radiation one obtains a more uniform and larger dosage to a greater depth.

DR. F. D. WEIDMAN: This is a large order — to open up the question of the basic metabolism of the skin—and I dare say that the reason for the use of hydrochloric acid was the work of Ellice McDonald, who claims to have demonstrated alkalosis of the blood in cancer. I recall that when Dr. Pfahler presented a large series of cases before the Philadelphia Dermatological Society, he brought out that point, but the p_H of the blood was not as consistently altered in different kinds of skin cancer as in visceral cancer. I felt at that time that the biology of cancer of the skin was something different — something that had to be approached from different angles than that of cancer which seems to have been established in the internal organs. It does not seem that there should be similar etiologic conditions operative in the skin in connection with all the different kinds of skin carcinoma. I greatly doubt that a blanket statement to the effect that there is an alkalosis or a deficiency of cholesterol in the skin can be held accountable for all the different carcinomas of the skin. My feeling is that when the last chapter in the etiology of cancer is written the causes of carcinoma will be about as diverse as those of tuberculosis, syphilis and leprosy.

LUPUS ERYTHEMATOSUS (BULLOUS TYPE) OR SENEAR-USHER PEMPHIGUS. Presented by DR. EUGENE TRAUB and DR. C. S. WRIGHT.

M. B., a white woman, aged 62, presented numerous erythematous patches suggestive of lupus erythematosus on the face. A patch 1½ inches (3.8 cm.) in diameter in the scalp showed atrophy and loss of hair. Scattered over the trunk and extremities were many lesions in which the skin was denuded. These clinically looked like neurotic excoriations. Subsequent observations showed the lesions on the face to be evanescent, at times almost disappearing. The lesions on the body remained unchanged except that new ones occasionally developed. No distinct bullae had been seen recently.

Microscopic examination of an infiltrated lesion on the forearm showed epidermis that was rather thick and acanthotic, covered by a nonparakeratotic corneum where it was still attached to the underlying corium. Where it was separated, the separation was between the epidermis and the corium, and in many places the papillary bodies still existed. In this area the blood vessels were increased in number and there was a dense round cell and connective tissue infiltration. A bullous lesion on the right shoulder showed a piece of tissue with only part of the epidermis attached to the underlying corium. In the section there was a small piece of epidermis. In some of the section it looked as though the remaining epidermis had been removed as the cover of a vesicle, because there were some strands of serum between the separated epidermis and the underlying corium. The base of this vesicle was corium and in this area the connective tissue nuclei were marked. A few round cells were scattered through this area, especially about the blood vessels. Where the epidermis was attached there was only slight infiltration about the blood vessels.

The eruption began in July, 1929, as bullous lesions over the back. Soon lesions appeared on the face, arms and legs. The patient then went to the Skin and Cancer Hospital in New York, where she was given boric acid ointment for local application and intravenous injections of iron cacodylate. Since coming to Philadelphia she had received three injections of gold and sodium thiosulphate, in doses of 5, 10 and 15 mg. respectively. The lesions on the face were distinctly better, but this could probably be attributed to the evanescent character of the eruption.

SENEAR-USHER PEMPHIGUS. Presented by DR. V. C. GARNER.

S. I., a white man, aged 28, presented erythematous lesions on the face of a butterfly configuration, with associated follicular plugging, superficial, yellowish erythematous, macular lesions over the presternal region and keratotic vesicular and bullous lesions over the midline of the back.

A biopsy on an early lesion showed an unruptured bulla with mild perivascular infiltration. A biopsy on a later lesion showed similar but more advanced changes. The blood count was normal except for a mild secondary anemia. The Wassermann test was negative. A Pels-Macht test showed 70 per cent.

The trouble began three and a half years before presentation, as an erythematous patch on the right cheek which responded to the intravenous use of gold sodium thiosulphate. The patient was free from lesions for one year; then the present outbreak occurred, which steadily progressed in severity.

DISCUSSION

DR. G. M. MACKEE: The interesting point is to decide whether there is a Senear-Usher syndrome as an entity, or whether the condition is pemphigus simulating lupus erythematosus or lupus erythematosus simulating pemphigus. In the cases shown today it seems to me that the evidence is all in favor of lupus erythematosus pemphigoides. Dr. Wise has written an excellent article on this subject. It will be instructive to hear his views.

DR. FRED WISE: I think that a number of these cases are difficult of interpretation, but the majority are actually lupus erythematosus with pemphigoid

lesions, in other words, disseminated lupus erythematosus pemphigoides. It would be interesting to find out, if possible, what the final results are in these cases. Is the outcome pemphigus, or is the outcome death due to lupus erythematosus disseminatus? I have yet to see one of these patients die of true pemphigus. The consensus in New York is the one which was expressed by Dr. MacKee, namely, that most of these are cases of lupus erythematosus. That is a logical conception, since the biopsy on the facial lesions showed the microscopic structure of lupus erythematosus and not of pemphigus. Now with respect to the biopsy of a bullous lesion, I understand that some of these cases present lesions which even under the microscope are tentatively diagnosed as pemphigus, but I think it would be difficult indeed for anybody to make a differential diagnosis under the microscope between epidermolysis bullosa, pemphigus and the Senear-Usher bulla without knowledge of the clinical picture. If I am wrong about that, I should like to be enlightened. I still believe that cases which do not present typical pemphigus, with its constitutional symptoms, loss of weight and, above all, pathologic apprehension, indicate that we are dealing with lupus erythematosus per se, which has become disseminated and in which the edema has caused an eruption of bullous vesicles, rather than true pemphigus.

DR. J. H. SWARTZ: Two years ago at a meeting of the Conference held in Boston, a similar discussion took place. The case in question was presented as one of probable pemphigus. The diagnoses suggested were lupus erythematosus and seborrheic dermatitis. Since then the patient has developed a typical case of pemphigus and a positive Pels-Macht test has been obtained. The present attack will probably terminate fatally.

DR. W. H. MOOK: Dr. Wise has discussed the case so thoroughly that there is very little to add. I agree with everything that he has said. Patients with lupus erythematosus may prove to have pemphigoid lesions. We studied twelve cases of disseminated lupus erythematosus, many of which showed the acute variety, and eight of the patients died; the other four cases belonged to the Senear-Usher type, and showed a course somewhat like that of the disseminated discoid type of lupus erythematosus. We have come to the conclusion that they belong to the lupus erythematosus class.

DR. J. J. ELLER: Did any of Dr. Mook's patients have a systemic tuberculosis?

DR. W. H. MOOK: No. None of those with the pemphigoid type of lesion. Some of the others, though, who died of acute lupus erythematosus had tuberculosis. We do not think that tuberculosis had anything to do with the condition.

DR. J. J. ELLER: About two years ago there was an article in the *British Journal of Dermatology* on erythema multiforme bullosum in which some of the author's cases described in this category are similar to the case shown here today. He found a systemic tuberculosis in several such cases.

DR. H. H. HAZEN: A number of years ago I had reason to believe that there was no such disease as pemphigus, that in reality pemphigus represented a bullous eruption caused by an infection, either localized or generalized, or by intoxication of some type, but I am rather inclined to feel that the foregoing discussion on the Senear-Usher type rather supports this view, in relation to one type of pemphigus at least. That is probably really another disease with a bullous manifestation. When we say pemphigus, we are discussing something which may not exist.

DR. I. R. PELS: Dr. Wise's remarks fill the requirements with regard to our conceptions of this syndrome, but I feel that they also demand a challenge on our part with regard to what we mean by this disease. They certainly offer a challenge to our conceptions of pemphigus, and should place us more in a position to differentiate the types of these two diseases.

With regard to the phytopharmacologic tests in which we are still much interested, we have found occasionally a fair number of positive readings in eruptions which challenge a definite classification, that is, in either pemphigus (not the Senear-Usher type) or the so-called disseminated lupus erythematosus. I prefer

to consider those in which there is no definite clinical basis for diagnosis under the group of toxic dermatoses or dermatoses of toxic origin, with an attempt to classify them thus if possible. The interesting thing to us is that we occasionally get a positive reading in such dermatoses when we cannot get a definite clinical history. Recently we had under observation a patient who died with a clinical lupus erythematosus disseminatus, with blebs here and there just before death, and who gave a positive reading. Occasionally, however, we get a normal reading in those cases. I feel that we may get some information if we do more of these tests, and I would request that we have more specimens sent for this test, particularly in those cases of Dr. Mook's type in which there is no definite clinical concept, but in which the patient is ill and apparently suffering from some toxemia. The test is still in a stage in which we cannot say that pemphigus always gives a positive reading. We occasionally get unexpected findings. We therefore can only offer the test for what it is worth.

DR. F. D. WEIDMAN: What sort of results have you obtained in bullous drug eruptions, a class of case in which the cause is very definitely known?

DR. I. R. PELS: I cannot answer that definitely, but I believe that in the main we get normal readings. I should add that in eruptions generally in which pemphigus or lupus erythematosus disseminatus acutus is not considered and in which we have a sick patient with an eruption that we cannot ascribe to drugs or to something definite, we occasionally get a positive reading.

DR. F. D. WEIDMAN: I take it that instances of bullous drug eruptions would be particularly illuminating in checking up as to whether you can ascribe a positive reading to any definite toxic features or not. Would samples of serum of previously proved bullous drug eruptions be helpful to you in estimating what the factors are that would or would not cause these positive phytopharmacologic reactions?

DR. I. R. PELS: We should be glad to have some of those specimens. It is possible that we might obtain positive tests in those cases in which our precautions are not observed. For example, the use of iodine or denatured alcohol in cleaning the arm and the placing of specimens of blood in oxalate or some other preservative will give a false positive test.

DR. FRED WISE: With respect to the remarks made by Dr. Hazen, it seems to me that we must emphasize one fact about the difference between the Senear-Usher syndrome and other diseases, and that is the indisputable findings on histologic examination. Have we a disease that begins as lupus erythematosus and eventuates in pemphigus, or are we dealing with a disease that is always pemphigus? The mere fact that the primary lesion is not one of pemphigus and frequently has been shown to be one of typical lupus erythematosus seems to me to be an argument against any other diagnosis than lupus erythematosus, unless we accept the possibility that patients with lupus erythematosus get pemphigus of a certain variety, as a secondary phenomenon, following or accompanying lupus erythematosus.

SYRINGOMA. Presented by DR. D. M. PILLSBURY.

This case was reported in the ARCHIVES in the April, 1932, issue, p. 738.

DISCUSSION

DR. F. D. WEIDMAN: The thing that struck me in the section was the hypoplastic character of the sebaceous glands even before roentgen treatment. We cannot ascribe the hyperplasia of the sebaceous glands to the effect of roentgen therapy. I take it that in this case we have an interesting combination of congenital defect of both sebaceous and sweat apparatus. The pearly appearance of some of the lesions in the scalp recalled the construction of benign cystic epithelioma, which likewise has a congenital basis. I think that this patient shows multiple nevic abnormalities and not simply syringoma.

CASE PRESENTED FOR DIAGNOSIS. Presented by DR. F. W. WEIDMAN.

L. J., a white woman, aged 39, was admitted to the Philadelphia General Hospital complaining of grip. There was a large area of extremely superficial scaliness over the right thigh. This scale was so thin that the finer markings of the skin were visible through it. It was tightly adherent except at the edges, where there was a thin, delicate, upturned collarette. There was no erythema associated with the scaliness. The scaliness was arranged in patches or bands, producing a general broad reticular effect. Between the bands, where the surface of the skin was sound, vague erythematous deep-seated nodules as large as a pea could be felt.

The patient had mild diabetes mellitus and chronic alcoholism. She was not able to give a reliable history.

DISCUSSION

DR. J. E. LANE: I think that there is a possibility of heat pigmentation, an erythema ab igne.

DR. FRED WISE: On careful examination and stretching the skin on the thigh, I thought atrophy was quite apparent. In the areas of atrophy there was a distinctive shiny appearance. That, in addition to the pigmentation which was mentioned by Dr. Lane and the presence of nodules in the skin which were described by Nobel, leads to the diagnosis of superficial lichenoid scleroderma, and I think that I am safe in saying that a histologic examination would reveal the structure of scleroderma.

PERIARTERITIS NODOSA. Presented by DR. F. D. WEIDMAN, from the medical service of DR. THOMAS B. KLINE.

P. M., a white man, aged 27, presented over the entire body dusky and moderately tender nodules ranging in size from 2 to 6 mm. In addition there was an infiltrated nodular patch on the neck and over each shoulder. More recently deep nodules had developed in the right sternocleidomastoid muscle and the right biceps. Other crops of erythematous nodules had appeared from time to time at varying intervals, with later regression.

The onset appeared as soreness and tenderness over the shoulders and left side of the chest, following an alcoholic debauch seven months previously. Subsequently the patient had pains in the calves which necessitated his going to bed. The leukocyte count had been as high as 22,000. The Wassermann reaction and blood cultures were negative. Streptococcus viridans and the pneumococcus had been isolated from the tonsils. The total protein content of the blood was 5.98 per cent; the chloride content, 722 mg.; clotting time, five minutes. A biopsy showed infiltration of polymorphonuclears around the capillaries, together with hyaline degeneration of the blood vessel walls. The picture was almost identical with what we have seen in erythema elevatum diutinum.

DISCUSSION

DR. G. M. MACKEE: This is the most interesting case demonstrated at this remarkable clinic. It is unique in my experience. I noticed on the history chart that Dr. Weidman correctly states that this is the first time our attention has been called to the skin manifestations of periarteritis nodosa. To a slight extent the lesions suggest a nodular iododerma, but I understand that Dr. Weidman definitely excluded the possibility of this cause. Histologically, of course, the condition is periarteritis nodosa.

DR. F. D. WEIDMAN: My interest in this case was in connection with erythema elevatum diutinum, and I believe that this case of periarteritis nodosa ought to be included in the general broad group of rheumatic dermatoses. I think that in the future when dermatologists meet with what appear to be atypical instances of rheumatic nodules or of erythema elevatum diutinum they should think of another member of this group, namely, periarteritis nodosa.

LUPUS ERYTHEMATOSUS OF THE CONJUNCTIVA; ARGYRIA. Presented by DR. J. V. KLAUDER.

M. G., a white woman, aged 51, was first seen in March, 1932, when she presented lesions of lupus erythematosus involving the scalp, ears, conjunctiva and possibly the buccal mucosa, although some of the lesions on the buccal mucosa were white and linear, resembling lichen planus. The conjunctival lesions were treated as trachoma by ophthalmologists without avail. Argyrol was advised for the lesions in the mouth, and the patient continued to use it twice daily for five years. Argyria appeared about four years after argyrol was first used.

The patient was presented to show favorable results in the treatment of argyria with sodium thiosulphate.

DISCUSSION

DR. J. H. SWARTZ: We had a case that showed about 25 per cent improvement, and after that no effect at all until we got discouraged and gave up the idea of sodium thiosulphate.

PIGMENTATION OF GUMS. Presented by DR. F. D. WEIDMAN.

F. B., a white man, aged 68, presented bluish-black patches of pigmentation on the mucous membranes of the upper and lower lips; there was none elsewhere in the mouth. The pigmentation did not appear to be related to any particular tooth or groups of teeth.

The Wassermann reaction of the blood was negative. Examination of the blood, including that for stippling of red cells, gave negative results. The sections showed minute brown spherules in the corium, but none in the epidermis. The prussian blue test for iron gave negative results. The blood sugar content was 132 mg.; urea, 16.5 mg.

A reliable history could not be obtained, but apparently antisyphilitic drugs like mercury, bismuth, arsenic and silver had not been administered. Eight lower teeth had been extracted one year previously. One tooth was allowed to remain, but was extracted six months subsequently. The gum did not heal at the site of the last extraction, and while cancer had been suspected, this diagnosis was not confirmed even after three biopsies had been performed.

The patient's work consisted in putting iron ore in furnaces and riveting.

DISCUSSION

DR. F. D. WEIDMAN: The bluish-black discoloration certainly suggests a metallic factor in the case.

DR. HARRY WASSERMAN: I recently saw a patient who gave a history of a mother and an older sister having the same disturbance. Her lips had a queer cyanotic bluish appearance, and the same color also appeared on her face whenever she was a little disturbed or excited. The rest of her skin was unusually pale and looked as if she had a secondary anemia. The discoloration had been present as long as she could remember. She had another sister who was free from the trouble. The color could not be blanched, but the mucocutaneous border of both lips was a definite cyanotic blue, which color was intensified under emotional strain. There was no cardiac disturbance or suggestion of any possible circulatory disturbance. I think that it was a congenital localized pigmentary disturbance. This patient may be somewhat of the same group.

DR. H. M. ROBINSON: Anybody who treats a large number of syphilitic patients sees numerous blue pigmentations on the labial mucous membrane as well as on the gums. I had seven patients with the dark lead-gray color that Spiegel reported, following the treatment with bismuth and silver arsphenamine. We never followed our cases through, but four patients had, in addition to a leadlike color of the skin, deep bluish pigmentary areas on the buccal surfaces as well as on the gums. We did not attempt to find out whether there had been any bismuth in those areas.

DR. J. J. ELLER: This pigmentation may be due to lead, bismuth or silver, as well as mercury, and I suggest that a section be taken and a spectroscopic examination made to determine if a metal is the cause, and which one.

DR. G. M. MACKEE: The pigmentation may be due to metallic deposits. This case recalls a patient whom Dr. Fordyce presented years ago who had pigmentation of the same color and of about the same extent, but on the side of the tongue. Unfortunately a biopsy in that case was impossible, and an examination for metallic deposits was not made. Dr. Fordyce regarded the condition as a pigmentary nevus of the mucous membrane. The patient, as far as he could remember, had always had it. The history here is unreliable, and recalls the case that I have just mentioned. Keeping in mind the sharp limitation of this pigmentation, I am inclined to agree with Dr. Wasserman that we must consider the possibility of a nevus as well as a metallic deposit. A phenolphthalein pigmentation should also be excluded.

DR. F. D. WEIDMAN: That localized effect prompted thoughts of Lain's work on electrolytic reactions of fillings in the teeth, but here again we could not get a history of fillings prior to extraction. That is a point which should be remembered; also the possibility of sulphur compounds coming out from the vulcanized substance that dentists use — sulphur in combination with rubber. I propose to go ahead with the microchemical analysis in this case.

DR. J. J. ELLER: We have a patient with mild argyria and no history of ingestion of drugs. Following the work suggested by Everett Lain, we had some galvanic measurements of the mouth of this man, who had various silver and gold fillings. There was a difference of one-quarter of a volt potential between some fillings that were side by side. The fillings were taken out and measurements are being made to determine exactly how much silver was dissolved. The claim was made that even a small amount of silver in colloidal solution may be deposited in the tissue and give a mild argyria. The case is still under investigation, and such a cause has yet to be proved.

DR. M. J. STRAUSS: I am sorry that I did not hear the beginning of this discussion, as I may be repeating what has already been said in regard to pigmentation of the gums and lips in Negroes. Of course there is a question as to whether or not it may be due to bismuth or mercury, but Dr. Anderson of the dental department of the Yale Medical School recently called my attention to pigmentation that was similar in appearance and location to that in the case presented here. He says that this is very common in any of the dark races, irrespective of the administration of any of the heavy metals.

CASE PRESENTED FOR DIAGNOSIS. Presented by DR. F. D. WEIDMAN and DR. R. L. GILMAN.

V. D., a white woman, aged 34, presented an extensive maculopapular eruption on the shoulders, back, and chest. The lesions were but slightly raised, and appeared to be somewhat grouped in scratch lines. The patient was an institutionalized mental defective with chronic pulmonary tuberculosis.

The Kolmer, Wassermann and Kahn tests were negative. No history of the ingestion of drugs was obtainable.

DISCUSSION

DR. FRED WISE: The lesions especially those of the back, undoubtedly resemble a papulonecrotic tuberculid of the large papular variety. It seems to me that, aside from the histologic examination which is indicated, the tuberculin tests will be of some value in the interpretation of these lesions. In addition, the patient has a considerable number of scars which are much lighter in color than the surrounding normal skin, which as a whole make one think of a papulonecrotic tuberculid rather than any other eruption except possibly a drug eruption.

DR. G. M. MACKEE: The case impresses me as being one of neurotic excoriations or perhaps malingering. I cannot make the differentiation without knowing

more of the history. If the patient admits the excoriations, and excoriates every little projection on the surface of the skin, as I suspect, the lesions are neurotic excoriations — a neurosis. On the other hand, if she denies traumatizing the skin, the condition is a psychosis and falls under the head of malingering. In any event, the eruption looks to me like a dermatitis artefacta.

DR. W. H. MOOK: This looks to me like a typical case of neurotic excoriations, as described so well by Pusey. Practically all of his cases were in neurotic persons, and we frequently see them in mental institutions.

DR. J. J. ELLER: I suggest Duhring's disease on account of the pigmentation and distribution over the back.

DR. P. E. BECHET: I am inclined to agree with Dr. MacKee about this case. The whole appearance of the eruption is artificial; there is no central necrosis. The lesions seem to be scooped out with the nail. It is not uncommon to see pigmentation and scarring from picking. The woman is a neurotic and mental defective and I think that the most probable diagnosis is neurotic excoriation rather than malingering.

DR. J. E. LANE: There are no scratch marks or itching, and there is to my mind no question that a large part of the lesions have been made by her picking. Whether there is any underlying disease or not I do not know, but I doubt it.

DR. F. P. MCCARTHY: The condition looks to me like a tuberculid plus neurotic excoriations.

DR. J. H. SWARTZ: The nurse stated that she observed the patient's skin closely and noticed that the skin was absolutely normal before the patient got at it. The nurse insisted that the lesions appeared after the patient picked and scratched. I believe that this would favor the diagnosis of neurotic excoriation.

CUTANEOUS TORULOSIS IN A MONKEY. Presented by DR. F. D. WEIDMAN.

The monkey on exhibition (under amytal anesthesia) presented a disease of three weeks' duration. Sections and cultures were also exhibited.

DISCUSSION

DR. F. D. WEIDMAN: I have never seen an instance of cutaneous torulosis in a human being, and in my search through the literature I only found two cases; only one was thoroughly described.

DR. W. H. MOOK: Five months ago a man was admitted to Barnes Hospital in St. Louis in a semiconscious condition. He was in the neurology service of Dr. Ernest Sachs. The intern noticed an elevated lesion on the sole of one of the feet, a typical infectious granuloma, about one quarter of an inch (0.6 cm.) in diameter, rather conical and crusted. I diagnosed it as an infectious granuloma, probably due to trauma. About a week later they operated on the brain lesion and found a pure culture of Torula. A culture was then taken from the lesion diagnosed as ordinary infectious granuloma, and it showed Torula. Clinically it could not be differentiated from an ordinary infectious granuloma.

CHRONIC TUBERCULOSIS OF THE SKIN. Presented by DR. ABRAM STRAUSS.

B. J., a Negress, aged 42, presented chronic tuberculosis of the skin over the face and extremities of seven years' duration. The eruption started as white infiltrated spots, which later became fungating and elevated. The patient was treated with neoarsphenamine with no result.

The Wassermann reaction of the blood was four plus. The biopsy showed the presence of numerous small foci made up of mononuclear cells and giant cells. Examination of the chest showed signs suggestive of tuberculosis. Roentgen examination showed lesions, not clearcut but suggestive of syphilis, in the area of the root of the left lung. There were no tubercle bacilli in the sputum. This patient subsequently died.

DISCUSSION

DR. J. E. LANE: I should classify the lesions on the body as lupus tumidus nonexedens.

PRIMARY INOCULATION TUBERCULOSIS WITH EXTENSION ALONG THE LYMPHATIC DRAINAGE AND SECONDARY SCROFULODERMA. Presented by DR. G. V. KULCHAR.

W. L., a colored child, aged 12 years, when first seen in the dispensary, on Dec. 30, 1931, presented slightly fungating granulomatous lesions over the right eyelid, right malar prominence and nasion. The borders were slightly raised and firm, and within the body of the lesions there were numerous old sinus openings, from which nothing could be expressed. The lesions were of a dull erythematous type, associated with superficial scaling. There was no definite contractile scarring. In addition, below the right mandible and over the region of the anterior cervical glands there were scars of an old lymphatic infection.

The Wassermann reaction of the blood was negative; a test with 0.01 mg. of old tuberculin gave slightly positive results; a biopsy showed foci of tuberculoid architecture with giant, epithelioid and small round cells high up in the corium and massive small round cell infiltration deep in the corum, with scattered giant cells. There were no fungi. Roentgen examination of the frontal bone gave negative results. No pus was obtainable at any time for staining or culture.

In 1928, the patient sustained a fracture of the frontal bone, and several months later this was followed by the appearance of granulomatous ulceration over the region of the fracture and subsequently over the right eyelid and the right cheek. In 1930, portions of the frontal bone were removed surgically. At this time surgical drainage of the anterior cervical lymphatics was done. In spite of local medication the lesions failed to heal.

Up to the time of presentation the patient had received fourteen injections of neoarsphenamine, during which time there had been about 40 per cent involution in all of the lesions. In addition, the Kromayer lamp had been used.

Book Reviews

Skin Diseases and Nutrition, Including the Dermatoses of Children. By Erich Urbach. Authorized English translation by F. R. Schmidt. Price, $7. Pp. 242, with 55 illustrations. Vienna: Wilhelm Maudrich, 1932.

This book gives a summary of all knowledge on the subject. It is a treasure house of information on diet in diseases of the skin. In a way it is a personal book, because the author freely gives his own experiences and his opinions based on them. It is also a review of the work of others. On the whole, it is conservative and temperate. The author, for example, is not able to cure psoriasis or acne with diet alone. On the other hand, in expressing the experiences of others, he gives startling statements of what they say can be done with diet. For example, others are quoted who have obtained good results in cases of keloid and elephantiasis with diet. Some of his own results are striking and thought-provoking, such as his results in some cases of lupus and eczema. It is a scholarly and scientific book — the work of a man who is trained in his field and who has given it deep study — and any one would be better for its careful reading, even though he may not always be able to go so far in his views of the effects of diet as the author.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. Frederick Burgess, President, Drummond Medical Bldg., Montreal.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Francis Eugene Senear, Chairman, 55 E. Washington St., Chicago.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee. Time: June 12-16, 1933.

American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.
Place: Chicago. Time: June 8-10, 1933.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry M. Robinson, President, 106 E. Chase St., Baltimore.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Emmett C. Troxell, President, 74 W. Adams St., Detroit.
William G. Saunders, Secretary, 9203 Grand River Ave., Detroit.
Place: Pittsburgh. Time: 1933.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 201 West Second St., Davenport, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Andrew L. Glaze, Chairman, 1928 First Avenue, Birmingham, Ala.
Dudley C. Smith, Secretary, University, Va.
Place: Richmond, Va. Time: November, 1933.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Frank Wilson, Secretary, 310 Greenleaf & Crosby Bldg., Jacksonville, Fla.
Place: Jacksonville, Tampa, Miami and place of meeting of state medical society.
Time: Quarterly.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Herbert H. Baukus, Secretary, 925 Delaware Ave., Buffalo.

Medical Society of the State of Pennsylvania Section on Dermatology

Stanley Crawford, President, 200, 9th St., Pittsburgh.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

G. H. Belote, Chairman, 201 S. Main St., Ann Arbor.
A. R. Woodburne, Grand Rapids Clinic, Grand Rapids.
Place: Grand Rapids. Time: Sept. 12-14, 1933.

Minnesota Dermatological Society

E. Z. Shapiro, President, 14 W. Superior St., Duluth.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

William E. Eastland, President, 117 N. Broadway, Oklahoma City.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

Texas Dermatological Society

T. J. Calhoun, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Adolph Rostenberg, Chairman, 152 E. 179th St., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

Brooklyn Dermatological Society

Louis J. Frank, President, 1367 Eastern Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo Dermatological Society

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Max Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Ralph R. DuCasse, President, Carew Tower, Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

E. W. Netherton, President, Cleveland Clinic, Euclid Ave. and E. 93d St., Cleveland.
H. G. Miskjian, Secretary, Rose Bldg., Cleveland.

Detroit Dermatological Society

Emmett C. Troxell, President, 74 W. Adams Ave., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Samuel Ayres, Jr., Chairman, 2007 Wilshire Blvd., Los Angeles.
Louis F. X. Wilhelm, Secretary, 1401 South Hope St., Los Angeles.

Manhattan Dermatologic Society

Fred Wise, Chairman, 200 West Fifty-Ninth St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

J. F. Burgess, President, Drummond Medical Bldg., Montreal, Canada.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

A. Benson Cannon, Chairman, 371 Park Ave., New York.
Louis Chargin, Secretary, 1 W. 85th St., New York.

New York Dermatological Society

George M. MacKee, President, 200 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Omaha Dermatological Society

H. C. Sumney, Chairman, 1011 W. O. W. Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Frederick D. Weidman, Chairman, 1930 Chestnut St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

Claude B. Norris, Chairman, 244 Lincoln Ave., Youngstown, Ohio.
Frederick Amshel, Secretary, 3401 5th Ave., Pittsburgh.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Ernest K. Stratton, President, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.